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TRAUMATIC RUPTURE OF THE NORMAL AORTA IN YOUNG ADULTS

REPORT OF TWO CASES

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TRAUMATIC rupture of the thoracic portion of the normal aorta in young adults is rare. The literature reveals many instances of rupture of different portions of the aorta in older age groups; the majority of these were associated with extrinsic erosions, inflammation, degeneration, and trauma, and a few occurred where there were structural abnormalities such as hypoplasia and coarctation. Two cases of complete rupture of the healthy thoracic aorta are reported in this paper; both occurred as a result of automobile accidents within two weeks of each other. We shall also discuss a few cases, reported in the literature, in which traumatic rupture of the normal aorta at the same site occurred in young adults. This age group, of course, includes the majority of the Armed Forces, and in this group the least degenerative changes are likely to have taken place.

Griffiths,[1] in 1931, described the case of a man, 26 years of age, who was dead when admitted to the hospital. According to his history he had been involved in a motorcycle accident. At necropsy a T-shaped rupture of the aorta just beyond the origin of the great vessels was found, which places the site of this rupture almost in the same area as in the two patients observed by us. Kleinsasser,[2] in 1943, reported the case of a man, 36 years of age, who, while walking, had been struck by a truck and thrown 30 feet. He was dead on admission to the hospital. At post-mortem examination the aorta was found to be incompletely severed at the junction of the aortic and thoracic portions. Some other interesting examples of traumatic rupture of the healthy aorta at the same and other sites in a little older age group are also reported here: Copeland's[3] patient was a 40-year-old man with rupture of the descending aorta; Kuhn's[4] patient was a 49-year-old man with "rupture of the lining of the aorta just as it springs from the left ventricle of the heart." This man did not die for ten days after the trauma which resulted in aneurysm and rupture. Kemp[5] reported the case of a 46-year-old man with a transverse tear of the aorta just beyond the line of the aortic valve. Jaffe and Sternberg[6] and Shennan[7] found in aviators who had fallen from various heights, transverse aortic lacerations near the ligamentum arteriosum and the great arterial trunks.

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ANATOMY OF AORTA

Consideration of the anatomy of the aorta in this area shows that the descending aorta is divided into two portions, the thoracic and the abdominal, in topographical correspondence with the two great cavities of the trunk in which it is situated.[8] The arch of the aorta ends at the left side of the lower border of the fourth thoracic vertebra, and the diameter in this portion is about 23 millimeters.[9] The thoracic aorta is situated in the posterior mediastinal cavity. It begins at the lower border of the fourth thoracic vertebra, where it is continuous with the aortic arch, and ends in front of the lower border of the twelfth vertebral body at the aortic hiatus in the diaphragm.[8]

CASE REPORT

CASE 1.—A man, aged 32 years, was riding in a one-fourth ton "peep" which overturned. The vehicle rolled over once and then righted itself. The man was found dead, hanging from the vehicle with his feet caught under the dashboard, apparently having sustained the weight of the car on his body.

Autopsy.—External examination: The patient, a 32-year-old man, was well developed and well nourished; he had numerous linear abrasions over the anterior thorax and several contusions over each ilium. There was a marked depression on palpation in the region of the tenth thoracic vertebra with movement of the spinous process.

Internal examination: (1) Dorsal dissection: Incision was made over the spinous processes from the first cervical to the twelfth thoracic vertebrae, and the soft tissues were dissected away. There was a fracture of the spinous process of the tenth vertebra. (2) Ventral dissection: The body was opened by a Y incision. When the breast plate was removed, examination of the thorax revealed fractures of the third rib, right, anterior; the fifth rib, bilateral, anterior; and the eighth rib, right, posterior. There was no displacement of the fragments, but the intercostal muscles and the parietal pleura of the fifth and seventh intercostal spaces were lacerated. The heart was normal. The left thoracic cavity contained about 2,500 c.c. of blood and clots with the lung floating on the surface. The aorta appeared as a white tube cut cleanly at the junction of the arch and thoracic aorta lying within a mass of infiltrated, bloody, connective tissue. The rupture was at right angles to the length of the artery. The aorta appeared healthy, and the intima was smooth and devoid of dilatations and plaques. The lungs were normal; no fractures of the skull and no injury to the abdominal viscera was noted.

Microscopic Report.—Heart and great vessels: The myocardium showed no significant change. The aorta had areas of periadventitial hemorrhage. The aortic wall showed no significant abnormality.

The cause of death was rupture of the thoracic aorta with exsanguination.

CASE 2.—A man, aged 24 years, was riding in a light civilian automobile, which was traveling at a high rate of speed, and failed to make a curve on the road. The vehicle overturned several times; he was thrown through the left side of the windshield, hitting his head on the frame as he was catapulted from the car, and killed.

Autopsy.—External examination: Inspection revealed that the skull was laid open from the left orbit to the left occiput; the dura and the cortex of the brain were exposed, as the entire roof of the skull was broken off in one piece, resulting in multiple fractures of the bones of the left side of the face and skull. There were numerous abrasions on both sides of the chest at the nipple line and on both iliac crests.

Internal examination: The body was opened by a Y incision; examination of the thorax revealed fracture of the first, fourth, fifth, and sixth ribs at the right anterior portion of the chest; the first rib was the only one to pierce the right lung, causing a 2-cm. laceration at the very apex. The intercostal muscles and the parietal pleura were lacerated between the third, fourth, fifth, and sixth ribs on the left side. The left thorax contained about 600 c.c. of blood and several large blood clots. The heart was normal. The aorta was gaping with torn, jagged edges at the junction of the arch and the thoracic aorta. The rupture was caused by a transverse laceration completely severing the entire thickness of the vessel. The aorta was structurally normal, and there was no evidence of atheromatous degeneration. The lungs were healthy except for a small laceration in the right apex.

The liver presented multiple lacerations on both surfaces. No other abdominal viscera were injured.

Microscopic Report.—Heart and great vessels: There were no significant changes in the myocardium or aortic wall.

The cause of death was multiple skull fractures with maceration of the brain and rupture of the thoracic aorta.

DISCUSSION

The dynamics of rupture of the thoracic aorta of healthy young adults is of particular interest. A pressure of 1,000 mm. Hg was not sufficient to rupture the aorta of individuals between 20 and 40 years of age according to the studies of Klotz and Simpson,[10] although Oppenheim[11] reported that a pressure of 3,000 mm. Hg was sufficient to rupture the normal human aorta. These figures are no doubt high, since rupture of the aorta in normal healthy individuals probably occurs only when sudden terrific force is applied to the thoracic cage. This violent force may no doubt be either direct or the result of contrecoup. In our two cases an element produced by torsion of the head and trunk doubtless was an important factor in bursting the aorta.

The site of rupture in our patients was distal to the emergence of the major branches of the aorta which is the relatively mobile point of the thoracic aorta. It becomes apparent that a sudden blow displacing the thoracic structures might cause a rupture in this mobile section either by direct or contrecoup force. In both our patients there was fracture of a few ribs but displacement of only one on the right side. The normal thorax is not a rigid structure and can be compressed in almost any diameter, although since resiliance is high in this age group, such condition probably only added to the element of torsion to the thoracic contents. Wilson and Roome[12] feel that, if the blow is received at the beginning of diastole of the heart, the aorta is then completely distended with blood and rupture is more likely to occur. The opinion of Warfield[13] is that the important factor in traumatic injuries of the heart and the aorta or its root occurs in full inspiration and that the sudden compression of the chest finds the heart caught and held between the inflated lungs which may result in rupture of the aorta. It is of interest that, in traumatic dissecting aneurysm, the site of predilection of intimal rupture is usually at or near the attachment of the obliterated ductus arteriosus (Botallo), just above the aortic valve and commonly on the posterior wall, near the aortic attachment of the ligamentum arteriosum, which acts as another point of fixation. These areas of fixation favor Rindfleisch's[14] theory that fixation predisposes to injury and also Abbott's[15] belief that, in these regions, the aorta may be congenitally weak.

In light of the absence of abnormalities on macroscopic and microscopic study of the aorta of our two cases, it is clear that complete transection of all the coats of the aorta owing to trauma in these two young adults is in marked contrast to spontaneous rupture of the aorta resulting from a process described by Erdheim[16] as medionecrosis aortae idiopathica. The latter pathologic process may occur in young adults as shown by Taylor and Morehead.[17] It is of particular interest that Schnitker and Bayer[18] found in 580 recorded cases of dissecting aneurysm of the aorta that 24.31 per cent occurred in individuals under the age of 40 years. They felt that the lesion usually resulted from cystic necrosis of media.

We agree with the opinion of Collins and D'Alessio[19] that the clinical syndrome produced by rupture of the aorta following trauma is caused by

surgical shock, but measures directed at combating shock and supporting the circulation are fruitless. Injuries of the intrapericardial portion of the aorta have been amenable to repair because of the surrounding structures, but perforating types of injury to the extrapericardial portion usually result in early death. Dshanelidze,[20] in 1922, reported the successful suturing of a wound of the thoracic aorta. Blalock,[21] in 1932, successfully sutured an ice-pick wound of the intrapericardial portion of the ascending aorta in a Negro. Elkin's,[22] in 1941, also reported the successful suture of a wound of the ascending aorta produced by an ice pick.

SUMMARY

1. Complete rupture of the normal thoracic aorta in young adults is rare.

2. Traumatic rupture at the junction of the arch and the thoracic portion probably occurs, because this is the most mobile portion of the aorta.

3. Rupture probably results from a sudden terrific blow to the thorax with both direct and contrecoup forces plus sudden torsion of the head and trunk.

4. Two cases of traumatic rupture of the normal aorta involving the junction of the arch and the thoracic portion are reported.

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STUDIES CONCERNING THE ETIOLOGY AND PATHOGENESIS OF NEUROCIRCULATORY ASTHENIA

II. The Mechanisms Underlying the Giddiness Found in Patients With Neurocirculatory Asthenia

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INTRODUCTION

GIDDINESS was early recognized[1, 2, 3] as an occasional manifestation of neurocirculatory asthenia (NCA), and scarcely any comprehensive review devoted to this syndrome fails to mention the occurrence of this symptom. But if this phenomenon has been recognized universally, it has not been investigated satisfactorily in regard to the mechanism responsible for its production. Soley and Shock[4] described giddiness occurring in their patients after the induction of hyperventilation, and they implied that the alkalosis therein produced might have given rise to it. But sufficient evidence has been accumulated[5, 6, 7] to make it evident that, although hyperventilation may occasionally be found in NCA patients, it is not an initial etiological factor of any real importance in the production of the syndrome from which they suffer. MacLean and his associates[8, 9] have studied NCA patients and have suggested that the giddiness from which they suffer at diverse times might be due to a defect in the return of venous blood to the heart. Since no determinations of venous pressure apparently were taken during their experiments, no real evaluation of their findings is possible.

In the present communication, the results are given of studies made concerning the incidence and the pathogenesis of giddiness in a group of forty-one young soldiers (average age: 26 years) suffering from neurocirculatory asthenia. They indicate that this symptom results from physiologic dysfunction of the cardiovascular system of these patients. It was found, too, that this phenomenon could be reproduced experimentally in susceptible individuals if a particular type of physiologic dysfunction were produced in them.

EXPERIMENTAL OBSERVATIONS

In the group of forty-one patients studied, twenty-nine, or approximately 70 per cent of them, gave a history of experiencing frequently an unpleasant sensation, best described by the term giddiness. Questioning revealed that, although this sensation was experienced by some individuals under varied conditions, the majority of patients experienced their giddiness intermittently and only at those times during which they abruptly changed from the supine to the erect position.

In five of our patients however, giddiness invariably occurred each time they arose from the sitting or supine position. In three of these five patients, this constantly occurring sensation had become so severe that they took particular care to rise quite slowly from the supine or sitting position.

It was found that all giddy NCA patients differed clinically from patients with orthostatic hypotension in several important respects. For instance, the

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former type of patient never exhibited any localized or generalized deficiency in perspiration or hypotension, and the giddiness experienced was always transient, occurring immediately after arising and disappearing in five to ten seconds. Furthermore when giddiness was complained of by an NCA patient, it was observed that he also was suffering severely from other recognized symptoms and signs of the syndrome.

Preliminary studies were made on three of the five patients who, as related, invariably experienced giddiness on arising. These studies consisted of measuring their blood pressure, venous pressure, and pulse rate and observing the occurrence of giddiness before and during their assumption of the erect position after the supine position had been maintained for fifteen minutes. For purposes of control, the same four observations were made on NCA patients without giddiness and on four young normal individuals. The venous pressure was determined by means of a direct puncture of the right antecubital vein with an intravenous needle (18 caliber) attached by rubber tubing (30 cm. in length and 2 mm. in diameter) to a glass manometer (1 mm. in diameter). The entire apparatus was filled with 3.5 per cent sodium citrate solution. It was found that a stable determination could be obtained within ten seconds.

It was found (Table I) that, although the venous pressure fell about equally in the three groups on arising, giddiness was experienced only by the susceptible NCA patients. Quite significantly, too, it was observed (Table I) that, whereas the pulse pressure diminished but 33 per cent in NCA patients without giddiness and 17 per cent in normal individuals, it had diminished 78 per cent in the giddy, NCA patients. The pulse rate also had increased disproportionately in the giddy patients as compared with the changes in pulse rate of the other two groups.

The two remaining patients who invariably experienced giddiness on arising were examined fluoroscopically before and during their assumption of the erect from the supine position. Two NCA patients without giddiness and two normal individuals were likewise observed. It was noted (Table II, *B* and *C*) that the subjects not susceptible to giddiness on arising showed little change on fluoros-

TABLE I. THE HEMODYNAMIC EFFECTS OF ABRUPT CHANGE OF POSITION IN THE GIDDY NCA PATIENT, IN THE NCA PATIENT WITHOUT GIDDINESS AND IN THE NORMAL INDIVIDUAL

	SUPINE POSITION			ERECT POSITION		
CASE	BLOOD PRESSURE*	VENOUS PRESSURE†	GIDDINESS	BLOOD PRESSURE‡	VENOUS PRESSURE§	GIDDINESS
			A. Giddy NCA Patients			
AB	135/85	5.0	None	125/110	3.0	Severe
ADBC	115/80	---	None	110/105	---	Severe
ABCDE	120/70	8.0	None	105/95	0.0	Severe
Average:	123/78	6.5		113/103	1.5	
			B. NCA Patients Without Giddiness			
CDBA	125/70	10.5	None	115/85	5.0	None
BDAC	135/95	4.5	None	145/95	0.0	None
ADCB	120/75	9.0	None	110/90	6.0	None
ACBDE	115/75	---	None	115/95	---	None
Average:	124/79	8.0		121/91	3.6	
			C. Normal Individuals			
A-10	125/75	8.0	None	115/70	-1.0	None
A-11	120/70	8.0	None	115/80	6.0	None
A-12	110/80	---	None	120/84	---	None
A-13	135/80	---	None	130/82	---	None
Average:	122/76	8.0		120/82	2.5	

*Blood pressure in mm. of Hg obtained after patient was in supine position for fifteen minutes.
†Venous pressure in cm. of H_2O as obtained by direct puncture of the right antecubital vein.
‡Blood pressure taken immediately upon assumption of the erect position.
§Venous pressure taken immediately upon assumption of the erect position.

copy other than a slight increase in rate of cardiac contraction, but the two giddy NCA patients (Table II, *A*) not only showed a marked increase in rate of cardiac contraction but also a sudden, abrupt decrease in the width and in the pulsatile excursion of the pulmonary artery (conus) which lasted for several seconds. The pulmonary artery then widened and was observed to pulsate again; the heart slowed and contracted more vigorously. The two patients complained of their giddiness a few seconds after the pulmonary artery was seen to narrow; their giddiness was no longer felt after the pulmonary artery was observed to widen and pulsate normally again.

These findings of a marked decrease in pulse pressure together with fluoroscopic evidence of marked diminution in the width of the pulmonary artery and in its degree of pulsation in those NCA patients experiencing giddiness on arising suggested that not only were abnormal hemodynamics observed to be present before the onset of giddiness but also that these same hemodynamic abnormalities might have led to cerebral changes which in turn gave rise to the sensation experienced by these patients. However, besides the hemodynamic abnormalities occurring after abrupt change of position, the possibility existed that the vestibular apparatus also might have been reflexly stimulated in these giddy patients and that some activity set up in this organ by such stimulation might have induced the giddiness. The last possibility later was eliminated, for it was found that giddiness could not be produced in susceptible patients either by flexing and extending the head upon the trunk in the erect or supine position or by making the patient quickly assume the supine position after prolonged standing. In short, the primary mechanism responsible for the abnormal sensation experienced by the giddy NCA patient appeared to be connected with some hemodynamic dysfunction. What was still undetermined was whether there was an *abnormally* decreased return of venous blood to the heart when the patient arose (as is supposed to occur in the patient with orthostatic hypo-

TABLE II. THE FLUOROSCOPIC EXAMINATION OF THE GIDDY NCA PATIENT, OF THE NCA PATIENT WITHOUT GIDDINESS AND OF THE NORMAL INDIVIDUAL, DURING CHANGE OF POSITION AND DURING THE PERFORMANCE OF THE FLACK TEST

	ASSUMPTION OF THE ERECT FROM THE SUPINE POSITION				PERFORMANCE OF THE FLACK TEST*			
CASE	MEDIASTINAL COMPRESSION?	INCREASE IN HEART RATE?	DIMINUTION IN WIDTH OF PULMONARY ARTERY?	VISIBLE PULSATION IN PULMONARY ARTERY?	MEDIASTINAL COMPRESSION?	INCREASE IN HEART RATE?	DIMINUTION IN WIDTH OF PULMONARY ARTERY?	VISIBLE PULSATION IN PULMONARY ARTERY?
				A. Giddy NCA Patients				
BA	None	Marked	Marked	Very little	Marked	Marked	Marked	None
AB	None	Marked	Marked	Very little	Marked	Marked	Marked	None
DBCA	-----	------	------	----------	Marked	Marked	Marked	None
ABC	-----	------	------	----------	Marked	Marked	Marked	None
CABD	-----	------	------	----------	Slight	Marked	Marked	None
ABCD	-----	------	------	----------	Slight	Marked	Marked	None
BACD	-----	------	------	----------	None	Marked	Marked	None
ACBD	-----	------	------	----------	Slight	Marked	Marked	None
				B. NCA Patients Without Giddiness				
ABDC	None	Slight	None	Unchanged	None	Moderate	None	Unchanged
BDCA	None	Slight	None	Unchanged	Slight	None	None	Unchanged
BDAC	-----	------	------	----------	Slight	Slight	None	Unchanged
CDBA	-----	------	------	----------	Slight	Slight	None	Unchanged
				C. Normal Individuals				
R-8	None	Slight	None	Unchanged	Marked	Slight	None	Unchanged
R-7	None	Slight	None	Unchanged	Slight	Slight	None	Unchanged
R-6	-----	------	------	----------	None	Slight	None	Unchanged
R-5	-----	------	------	----------	Slight	Slight	None	Unchanged
R-4	-----	------	------	----------	None	None	None	Unchanged

*Observations made from beginning of Flack test up to twenty seconds of continuous blowing.

tension[8]), or whether there was an abnormal response of the cardiovascular system of the susceptible patient to the *normally* decreased return of venous blood to the heart which occurs on assumption of the erect from the supine position.

If the giddiness of the patients under observation arose from the hemodynamic effects originally initiated by decreased return of venous blood to the heart, such giddiness should be induced by any measure compressing the veins leading into the right auricle, thus inhibiting the venous return. To accomplish this reduction in venous return, a modification of the Flack test[10] was used in which the patient sustained a mercury column at a level of 30 mm. Hg for twenty seconds by blowing into a rubber tube connected to the bottom of the receptacle containing the mercury. A reduction in venous return to the heart was accomplished supposedly by the resulting increase in intrathoracic pressure.[8] The advantage of this test was that it entailed no change in position, thus eliminating possible influences upon the vestibular system and that it also allowed sufficient time for various hemodynamic measurements not able to be obtained in the previously described experiments.

Nineteen patients with neurocirculatory asthenia (twelve of whom gave a history of very frequent giddiness on arising) and eight normal individuals were tested in the erect position. Six of the twelve giddy patients were tested also in the supine position. The presence or absence of giddiness, the blood pressure, the venous pressure, and the pulse rate were determined before and during the performance of the Flack test. In some subjects, determination of the arm-to-tongue circulation time (calcium gluconate method) before and during the test also was obtained.

Table III, *A* reveals that each of the twelve NCA patients who gave a history of experiencing giddiness complained of the same sensation during the Flack test, and declared that it was identical with that which they usually had experienced on arising quickly. The control subjects, however (Table III, *C* and *D*), with the exception of two individuals (A-3 and A-8) experienced no subjective results other than a feeling of fullness in the head and neck during the test.

More important than the subjective sensations felt by these patients was the striking and differential reaction of their blood pressures during the test. For, although most NCA patients without giddiness and normal individuals showed either no change or a slight rise in their systolic pressures after twenty seconds of blowing (Table III, *C* and *D*), a very slight decrease in systolic pressure occurred in nine of the giddy NCA patients (Table III, *A*). More significant was the striking rise of the diastolic pressure in the giddy patient (average rise: 30 mm. Hg) during the test as compared to the rise in the NCA patients without giddiness (average rise: 14 mm. Hg) and that in the normal individuals (average rise: 17 mm. Hg). This marked increase in the diastolic pressure of the giddy patients during blowing resulted in an average pulse pressure of 8 mm. Hg (Table III, *A*) and explained the disappearance of the radial pulse observed and commented upon by Master.[11] The great enhancement and the slight diminution noted in diastolic and systolic pressures, respectively, of the giddy NCA patients during the Flack test must be taken as evidence that a marked peripheral arteriolar constriction must have occurred to have caused these pressure changes. It should be noted, finally, that these blood pressure changes occurring in the giddy NCA patient during the Flack test were similar to those observed when the same type of patient changed his position (compare Tables I, *A*, and III, *A*).

TABLE III. THE HEMODYNAMIC EFFECTS OF THE FLACK TEST IN THE GIDDY NCA PATIENT (IN ERECT AND SUPINE POSITION), IN THE NCA PATIENT WITHOUT GIDDINESS AND IN THE NORMAL INDIVIDUAL

	BEFORE FLACK TEST					DURING FLACK TEST*				
CASE	GIDDINESS	B.P.†	V.P.‡	PULSE§	CIRC. TIME‖	GIDDINESS	B.P.	V.P.	PULSE	CIRC. TIME
A. Giddy NCA Patients in Erect Position										
AB	None	145/90	9.0	88	13	Very severe	125/118	30.5	130	Over 30
BA	None	130/88	3.5	84	--	Very severe	125/122	25.0	144	----
ABC	None	110/70	8.0	86	--	Very severe	105/103	32.0	120	----
BAC	None	135/90	4.0	82	12	Very severe	160/150	28.0	132	Over 30
ABCD	None	125/85	5.0	90	11	Very severe	115/108	32.0	144	20
ACBD	None	110/70	6.5	84	--	Very severe	105/100	27.0	102	----
CABD	None	120/80	---	110	--	Very severe	122/118	---	132	----
BCDA	None	120/80	10.0	84	--	Very severe	118/110	31.0	100	----
ADBC	None	120/76	2.0	80	--	Very severe	112/105	24.0	120	----
ABCDE	None	130/85	---	90	--	Moderate	125/110	---	125	----
ACBDE	None	120/95	---	80	--	Moderate	125/110	---	122	----
ABCED	None	135/95	---	84	--	Very severe	125/118	---	120	----
Average:		125/84	6.0	87			122/114	28.6	124	
B. Giddy NCA Patients in Supine Position										
AB	None	140/80	10.5	80	--	Very severe	120/118	36.5	120	----
BA	None	125/80	8.0	80	--	Very severe	120/116	33.0	132	----
BAC	None	135/85	10.0	84	--	Very severe	150/145	34.0	128	----
ACBD	None	110/70	9.0	80	--	Very severe	105/95	32.0	110	----
ABCED	None	125/80	---	82	--	Very severe	138/132	---	118	----
ACBDE	None	125/80	---	76	--	Severe	125/115	---	116	----
Average:		128/81	9.3	80			126/120	33.9	120	
C. NCA Patients Without Giddiness in Erect Position										
ABDC	None	135/70	8.0	80	11	None	135/90	24.0	90	12
CDBA	None	130/80	8.0	80	--	None	140/90	22.0	85	----
BDCA	None	155/85	10.0	84	12	None	155/100	10.0	96	----
BDAC	None	145/95	2.0	96	--	None	155/105	21.0	132	----
ADCB	None	135/75	9.0	88	--	None	135/90	9.0	96	----
ACBED	None	115/75	2.5	72	--	None	115/95	10.0	132	----
R-1	None	125/80	5.5	--	--	None	125/90	8.0	---	----
Average:		134/80	6.4	83			137/94	14.8	105	
D. Normal Individuals in Erect Position										
A-1	None	130/80	6.5	84	12	None	125/90	10.5	92	13
A-2	None	135/90	8.0	80	10	None	133/102	10.0	108	12
A-3	None	125/70	6.0	70	--	None	135/100	32.0	90	----
A-4	None	115/80	6.0	80	--	None	125/90	16.0	88	----
A-7	None	105/80	4.5	88	--	None	130/105	15.5	96	----
A-8	None	115/85	7.0	84	--	None	130/105	29.0	94	----
A-9	None	120/90	2.0	76	--	None	120/105	18.0	90	----
A-10	None	115/65	---	--	--	None	120/80	---	---	----
Average:		120/80	5.7	80			127/97	18.7	94	

*All observations taken after twenty seconds of blowing.
†Blood pressure in millimeters of mercury.
‡Venous pressure (directly observed from right antecubital vein) in centimeters of water.
§Pulse rate per minute.
‖Circulation time (calcium gluconate method) from arm to tongue.

In preliminary experiments, during which the blood pressure measurements were made before and five, ten, fifteen, and twenty seconds after the beginning of the Flack test, it was found that the patients never experienced giddiness until their pulse pressures decreased below 20 mm. of mercury. It was found, in addition, that the intensity or severity of their giddiness was directly proportional to the decrease in pulse pressure. These observations suggested that peripheral arteriolar constriction preceded the giddiness and possibly played a part in the production of the sensation felt by these patients.

The venous pressure was obtained as previously described in the three groups of subjects. After the control level had been established (within ten seconds), the subjects began the Flack test with the pressure manometer still connected to their veins. It was observed that in all three groups, the venous

pressure began to rise after five seconds of blowing. After approximately fifteen seconds of blowing, however, the venous pressure of the normal subject and the NCA patient without giddiness ceased to rise and became relatively stable. However, the venous pressure of the giddy NCA patient was observed to continue to rise as long as the patient continued to blow against the mercury column, even if, as in some cases, the test continued for thirty seconds. The measurements of the venous pressure shown in Table III, *A*, *C*, and *D* (recorded after twenty seconds of blowing) indicate that the average venous pressure of the giddy NCA patient (28.6 cm. H_2O) was approximately twice as high as that of the NCA patient without giddiness (14.8 cm. H_2O) and considerably higher than that of the normal individual (18.7 cm. H_2O). It will be noted that in two of the normal subjects (Table III, *D*, A-3 and A-8), the venous pressure was high at the end of twenty seconds. Both of these individuals also were found to experience giddiness at this time. Since many an otherwise normal young adult will give a history of having experienced giddiness on arising, it is not surprising that considerable variation was found in the objective and subjective results of our control group of subjects, in relation to the venous pressure and sensation of giddiness. This rather suggests that the NCA patient with giddiness differs quantitatively, not qualitatively, from the average individual. However, the far greater average rise in venous pressure in the giddy NCA patient during the Flack test indicates that, in them, the venous flow was either abnormally increased during blowing or that the test produced a greater obstruction to venous flow in the mediastinum of the giddy NCA patient. In view of the fact that arteriolar constriction was present, it was assumed that there was a greater venous flow because of the consequent greater expulsion of blood from the arteriolar system, for no satisfactory reason could be found for assuming that the Flack test produced a greater mechanical obstruction in the mediastinum of the giddy NCA paient than it did in the mediastinum of the other types of subjects. It must be added, too, that perhaps there was constriction of the venules and capillaries in the giddy NCA patients during the test which would increase the venous flow also. However, no proof of this last assumption was able to be obtained.

When giddy NCA patients were compared with NCA patients without giddiness and with normal individuals under the fluoroscope before and during the performance of the Flack test, it was found that not only did the heart rate of the giddy patient increase abnormally as compared with the heart rate of the controls but also the pulmonary artery of the giddy patient was seen to narrow markedly and pulsatile excursions of the same artery could not be detected. In other words, the fluoroscopic observations of the giddy patient during blowing, like the blood pressure changes, were similar to those following change of position (Table II, *A*). About five seconds after the pulmonary artery was seen to narrow and apparently cease to pulsate, the patients complained of giddiness. When they ceased blowing, the pulmonary artery was seen to resume its normal size and action. After a few seconds, the patients stated that they were no longer giddy.

In connection with the fluoroscopic examinations, the determinations of the arm-to-tongue circulation time produced important results. For, whereas in two of the three giddy patients so tested (Table III, *A*) the arm-to-tongue time was less than thirteen seconds before blowing, no sensation could be perceived if the calcium gluconate were injected into the antecubital vein five seconds after blowing had begun even though the latter were continued for thirty seconds. This observation, when considered with the abrupt changes seen in the pul-

monary artery during blowing, indicated quite conclusively that during the test very little or no forward flow of blood occurred in these giddy patients; otherwise they would have felt the injected calcium either in their tongues or elsewhere in their bodies. When these same two patients ceased blowing, they felt the previously injected calcium in their tongues approximately six seconds after cessation of blowing. This last observation suggested that the blood containing the calcium had been impeded somewhere in the pulmonary circuit; otherwise the calcium would not have been felt in the tongue so rapidly after blowing had been stopped.

DISCUSSION AND SUMMARY

Since both the Flack test and abrupt change of body position presumably decreased the return of venous blood to the heart, temporarily at least, in all individuals, it was not surprising to observe that the objective and subjective results noted in the giddy NCA patients during the Flack test were similar to those following abrupt change of position. The intense pulmonic and systemic vasoconstriction observed in the giddy NCA patient in each type of test was not a reaction to an abnormally lessened venous return to the heart because it was found that the giddy patient during the Flack test showed a higher venous pressure in the antecubital vein than the normal individual, indicating that the venous return from the upper extremity at least was above normal. Furthermore, there was no abnormal decrease in venous flow from the lower extremities in these giddy patients for the hemodynamic and subjective reactions of six such patients (compare *A* and *B* of Table III) during the Flack test were qualitatively and quantitatively identical whether they performed the test in the erect or supine position. This would not have been the case if there were an abnormally lessened venous flow from the lower extremities in the erect position. For this reason it seems impossible to escape the conclusion that the temporary and intense pulmonic and systemic vasoconstriction observed during the Flack test was due to a fundamental hyperirritability of the cardiovascular system of these patients to slight changes in the flow or pressure of venous blood returning to the right auricle—changes which in the normal individual evoke only slight and physiologically commensurate readjustments in the cardiovascular system.

In a previous article,[12] the hyperthermia present in many NCA patients was described. It was deduced from these same studies that the hypothalamus was affected in some manner in these hyperthermic NCA patients. In the present studies, the profound and generalized vasoconstriction which occurred in the giddy NCA patient following maneuvers which caused no comparable effect in the normal individual suggests that the portion of the autonomic nervous system concerned with this vasoconstriction, namely, the sympathetic nervous system, was hyperirritable or deranged in the giddy NCA patient. Since the main coordinating center of this portion of the autonomic nervous system lies within the hypothalamus,[13] it is conceivable that this area of the brain may be involved in the pathogenesis of the giddiness found in the NCA patient. No direct proof, however, has been found to support this last conception.

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FURTHER EVIDENCE FOR THE PURELY VALVULAR ORIGIN OF THE FIRST AND THIRD HEART SOUNDS

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ALTHOUGH the fact that the first heart sound is of purely valvular origin is stressed in recent texts on physiology and on heart disease,[1] and has been borne out by many precisely recorded observations made recently, not all of the evidence in recent contributions has been emphasized in connection with this problem. On the other hand, evidence based on thoroughly unsatisfactory sound tracings has been interpreted as proving that there is an appreciable muscular element in the first and third sounds.[2, 3] For a correct understanding of physical signs, the matter is of sufficient importance to be discussed more fully. Most close students of heart sounds can agree with the discussion of the first sound presented by White and his colleagues,[1] based on their own work and on that of others. These careful students have found no evidence of audible vibrations due to the ventricular wall itself.

Smith[2, 3] and his co-workers present tracings of the movements of the ventricular surface of the dog's heart, some of which show, superimposed on the cardiogram, oscillations of low amplitude which undoubtedly are due to audible vibrations arising in the heart. These records all were obtained from the normally functioning heart. In these papers they present tracings obtained from the heart after cutting off venous inflow, filling the ventricular chambers with balloons, ligating around the A-V sulcus,[2] or immobilizing the valves with special devices introduced through the auricles.[3] None of these tracings show any vibrations of audible frequency, except possibly one with a balloon in the ventricles. As rubbing such balloons with a wet object is a standard trick in sound production, known to most children, this latter observation is not surprising and is irrelevant to a study of the heart sounds.

Movements of the heart wall, which for the most part appear as single swings away from the base line, with durations of 0.08 to 0.28 second, are marked as

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"sounds," and on the basis of this unwarranted identification it is concluded that significant elements of the first and third sounds originate in the ventricular wall itself.

Since 16 cycles, or double vibrations, per second is given as the lower limit of human hearing in audiometer tests, and since 12 cycles per second is accepted by physiologists as the lowest pitched sound ever audible to man, any such cardiac movements, with cycles of 6 to 1.8 per second, obviously are inaudible. It may be true that the authors heard "dull" sounds when they listened to binaural stethoscopes attached to their recording system as these records were being inscribed, but this merely proves that puffs of air, in a closed system, can set the eardrums in vibration.

Wiggers and his co-workers[4, 5] have carefully studied the recording of heart sounds, and have shown what acceptable records look like. They have recognized the artifacts produced by applying funnels or diaphragms directly to the heart, and by not having an open system to obviate mechanical pressure waves. All these precautions were ignored by Smith and his co-workers, and few of their records show adequate records of sounds, while movements of the heart lasting through half of the cardiac cycle are recorded as tall broad waves of far greater amplitude than any of the oscillations of audible frequency. Waves whose full cycle duration would be 0.16 to 0.56 second cannot be regarded as sounds, for which the shortest cycle length is, at most, 0.08 second.

Boyer[6] had already proved that the third heart sound originated in the heart and not, as had been suggested, from the heart's striking the chest wall. He showed that an oscillation of very low amplitude and frequency could be caused by the heart striking the diaphragm of the recording pickup, but this in no way resembled the third sound recorded from a cardiometer within which the heart was suspended so that it could not touch the walls (Figs. 2, *B* and 2, *C*[6]).

Lewis and Dock[7] had recorded silent ectopic beats which occurred 0.02 second after the second sound, and beats of similar electrocardiographic contour occurring 0.10 second after the second sound but associated with very loud first sounds. This proved that in man the first sound does not occur during a systole which precedes the opening of the atrioventricular valves. They had shown that third heart sounds which varied during respiration were associated with variable degrees of sudden diastolic retraction of the apex and presumably of reflux toward the auricle. Since the first and third sounds are indistinguishable in quality, and either may exceed the other in intensity, they concluded that the first and third sounds originated in sudden tensing of the atrioventricular valves, by systole or by reflux.

MacLeod and Cohn,[8] using a piezoelectric pickup and recording from the interior of the auricles and ventricles, showed that sound vibrations are recorded only very close to the semilunar cusps (second sound most intense) and in the atrioventricular opening (first sound only). Their system, designed to record pressure changes, is relatively insensitive to sound, and shows how rapidly the sounds fade as the pickup moves into either auricle or ventricle from the valve area. Thus, for the first time, the points of origin of the first and second sounds have ben sharply and surely defined (Fig. 3, *VI* and *X*[8]).

Dock[9] had already shown, using the recording system described by Wiggers, that the first sound of the dog's heart disappeared when the venous inflow was arrested or the atrioventricular valves were immobilized by ligatures. While Smith's records are unsatisfactory technically, they confirm these observations since the vibrations of audible frequency in early systole of the normally beating

heart, apparent in Fig. 2 *A*,[3] disappear at once on closing off the venous inflow (Fig. 2 *B*[3]). In Fig. 2 *B* et seq. only the cardiogram, with oscillations of far less than audible frequency, remains. Thus Smith's experiments actually confirm those done with appropriate methods of recording heart sounds.

It cannot be too strongly urged that those who study heart sounds filter out the mechanical oscillations as far as possible, and that only double vibrations lasting 0.06 second or less be regarded as sounds. Experience has shown that gallop phenomena can be recorded when they are inaudible, so that in clinical study records of the vibrations of small intensity or subaudible pitch may be of real value.

It is extremely doubtful whether the ear ever detects the vibrations arising in the auricles and great vessels just before and after the main vibrations of the first sound.[1] It is certain that variations in intensity and quality of the apical first sound are closely related and probably due to variations in the intensity and synchronization of the vibrations which arise in early systole from sudden tensing of the right and left atrioventricular valves. Clinically then, the first sound is purely valvular.

CONCLUSIONS

By recording sounds from the interior of the dog's heart, MacLeod and Cohn sharply localized the atrioventricular valves as the site of origin of the first sound and the semilunar valves as the site of origin of the second. Rapid vibrations also were recorded near the semilunar valves very early in systole.

The site of origin of the third heart sound has not been determined with precision, but as the sound occurs in normal dogs given rapid saline infusions, the technique of MacLeod and Cohn can easily be applied by those who doubt the evidence, from observations on man, that this sound also arises in the atrioventricular valves. No experimental or clinical proof that any element of any of the normal sounds has its origin in the ventricular wall has yet been presented.

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THE INTRAVENOUS ADMINISTRATION OF LANATOSIDE C TO PATIENTS TAKING MAINTENANCE DOSES OF FOLIA DIGITALIS UP TO THE DATE OF HOSPITALIZATION WITH RECURRENT CONGESTIVE HEART FAILURE

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INTRODUCTION

IT HAS been suggested by Gold and DeGraff[1] that patients with auricular fibrillation need larger maintenance doses of digitalis when they are on the verge of, or in, congestive heart failure. Fahr and LaDue[2] demonstrated the need for higher maintenance doses of lanatoside C during the period of failure in patients with auricular fibrillation. Eight patients required an oral dose of 2.5 mg. to keep the heart rate below 80 while signs of heart failure were present, but 1 mg. to 0.5 mg. sufficed when these patients had established compensation. As yet, we have no adequate means of determining whether the patient with heart disease associated with regular sinus rhythm is receiving maximal therapeutic doses of digitalis. It seemed worth-while to us, therefore, to determine the therapeutic and toxic effect of the intravenous administration of lanatoside C (Cedilanid) to patients who developed congestive heart failure while taking maintenance doses of 0.1 to 0.3 Gm. of folia digitalis.

Many authorities strongly advise against the intravenous administration of cardiac glycosides to any patient who has taken digitalis within the preceding ten days,[3] since uncontrollable nausea and vomiting, extrasystoles, pulsus bigeminus, ventricular tachycardia, ventricular fibrillation, heart block, or cardiac standstill may result.

However, during the course of a previous study,[2] intravenous injections of lanatoside C were given without toxic manifestations to several patients who erroneously denied previous digitalis dosage. Hence, we decided that this problem was worthy of further study.

METHOD

Thirty-one patients with congestive heart failure were given 0.8 mg. (half the digitalizing dose[2]) of lanatoside C intravenously, despite the fact that they had been taking 0.1 to 0.3 Gm. of folia digitalis daily for periods of weeks or months before the current admission. Twenty-two patients were given 1.2 mg. of lanatoside C. intravenously, and nine patients received 1.6 milligrams. Of these sixty-two patients, thirteen had auricular fibrillation with apical pulse rates from 90 to 140, and forty-nine had congestive heart failure associated with regular sinus rhythm. All had venous pressures greater than 15 cm. of water on admission, and most of them had heart failure of high degree.

Fifty-one of the patients were between the ages of 41 and 80 years; thirty-seven were colored, and twenty-five were white. Forty-one had hypertensive heart disease; eleven had arteriosclerotic heart disease; eight had syphilitic heart disease; and two had rheumatic heart disease.

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Daily measurements were made of the venous pressure, vital capacity, and circulation time; the degree of pulmonary and peripheral congestion; the degree of dyspnea, orthopnea, and cyanosis; together with clinical notes concerning the heart rate, rhythm, and size, as well as the subjective state of the patient. No diuretics or other drugs were given except sedatives as needed for rest or relief of cough or pain. Fluid and salt intake was not restricted. Electrocardiograms were made on admission and the day after the intravenous administration of lanatoside C when possible. Maintenance doses of from 0.1 to 0.3 Gm. of folia digitalis were started six to twelve hours after the injection of the cardiac glycoside.

RESULTS

Table I summarizes the data obtained from all sixty-two patients. Thirty-six of the forty-nine patients with heart failure associated with regular sinus rhythm responded to the medication with a prompt stabilization of the venous pressure within two to six days. By stabilization we mean that the venous pressure fell significantly, reaching 10 cm. of water or lower, and the circulation time fell to a constant level, usually 16 to 28 seconds. In every instance, the previously elevated venous pressure and circulation time fell to levels approaching normal.

TABLE I*

NUMBER OF PATIENTS WITH				DOSAGE OF LANATOSIDE C	DAYS FOR STABILIZATION OF CERTAIN CRITERIA OF CONGESTIVE HEART FAILURE			NUMBER OF PATIENTS		
AURICULAR FIBRILLATION	REGULAR SINUS RHYTHM	ECG EVIDENCE OF DIGITALIS		(MG.)	CIRCULATION TIME	VENOUS PRESSURE	DYSPNEA AND ORTHOPNEA	SHOWING NO IMPROVEMENT	WITH TOXICITY	FATALITIES
		BEFORE	AFTER							
6	25	9	10	0.8	6.6	2.0	5	3	0	5
6	16	12	7	1.2	5.8	6.8	4	2	1	4
1	8	3	3	1.6	5.0	6.0	4	0	0	2

*This is a summary of the data obtained from all sixty-two patients studied. See text.

TABLE II*

PATIENTS WITH AURICULAR FIBRILLATION	DOSAGE OF LANATOSIDE C (MG.)	VENTRICULAR RATES				DAYS FOR STABILIZATION OF CERTAIN CRITERIA OF CONGESTIVE HEART FAILURE			NUMBER OF PATIENTS		
		120-140	100-120	90-100	60	CIRCULATION TIME	VENOUS PRESSURE	DYSPNEA AND ORTHOPNEA	SHOWING NO RESPONSE	WITH TOXICITY	FATALITIES
6	0.8	1	2	2	1	6.5	7.0	6	2	0	0
6	1.2	3	3			5.0	5.6	4	0	0	1
1	1.6		1			5.0	5.0	4	0	0	0

*This is a summary of the data obtained from thirteen patients with auricular fibrillation. See text.

TABLE III*

PATIENTS WITH REGULAR SINUS RHYTHM	DOSAGE OF LANATOSIDE C (MG.)	DAYS FOR STABILIZATION OF CERTAIN CRITERIA OF CONGESTIVE HEART FAILURE			NUMBER OF PATIENTS		
		CIRCULATION TIME	VENOUS PRESSURE	DYSPNEA AND ORTHOPNEA	SHOWING NO RESPONSE	WITH TOXICITY	FATALITIES
25	0.8	5.8	7.1	4.4	1	0	5
16	1.2	5.5	5.8	4.2	2	1	3
8	1.6	8.7	8.0	6.0	0	0	2

*This is a summary of the data obtained from forty-nine patients with regular sinus rhythm. See text.

Tables II and III present the same data separately for patients with auricular fibrillation and for patients with regular sinus rhythm. Most of the discussion in the text, except as noted, refers to Table I.

If we compare the rapidity of response in these patients (all had initial venous pressures above 15 cm. of water) with that of a previously studied group of patients with regular sinus rhythm (Table IV), it will be seen that the venous pressures of the thirty-six patients now under discussion fell much more rapidly than did those of a "control group" of patients with comparable degrees of heart failure who were given no digitalis. This control group was a series of twenty-four patients who received no cardiac glycoside during their hospitalization. We feel, therefore, that the response of these thirty-six patients could not be attributed to bed rest alone.

TABLE IV. NORNAL SINUS RHYTHM*

THERAPY	TOTAL NO. OF CASES	AV. NO. OF DAYS FOR VENOUS PRESSURE TO FALL TO 8 CM. WATER	AV. NO. OF DAYS FOR ONSET OF DIURESIS	AV. NO. OF DAYS FOR SIGNIFICANT RISE —30%— IN VITAL CAPACITY	AV. NO. OF DAYS IN BED	AV. NO. OF DAYS IN HOSPITAL	MORTALITY %
Venous Pressure > 15 Cm. of Water							
Control	24	14.8 (14)	6.4(12)	13.0(11)	24.1(12)	27.4(13)	41.7
Lanatoside C	54	4.5 (39)	3.3(31)	8.5(32)	12.2(33)	19.5(27)	25.9
Venous Pressure < 15 Cm. of Water							
Control	18	3.7 (12)	3.3(11)	11.6(9)	10.3(12)	18.4(14)	22.2
Lanatoside C	11	2.1 (10)	3.0(6)	6.2(6)	11.4(11)	18.8(11)	0.0
Lanatoside Delayed							
Control period	21	>17.1 (16)	>17.1(16)	>17.1(16)			
After lanatoside	21	3.1 (16)	3.0(13)	7.3(11)	10.4(13)	19.7(12)	23.8
VENOUS PRESSURE		AURICULAR FIBRILLATION					
>15 cm. of water	67	3.4 (47)	2.3(38)	8.0(40)	15.6(34)	25.7(30)	22.4
<15 cm. of water	35	2.8 (8)	2.3(13)	10.5(13)	15.2(24)	23.9(21)	11.4

*This is a summary of data previously obtained from 188 patients with congestive heart failure.[3] None of these patients had taken digitalis for at least three weeks before hospital admission, and all received lanatoside C within twelve to twenty-four hours after entering the hospital except in the Lanatoside Delayed series. Patients in this series were given the drug after an average of seventeen days in the hospital without digitalis therapy. The numbers within parentheses indicate the total number of cases from which each average used in the statistical analysis was obtained. The average number of days is reckoned from the time of admission to the hospital in all cases except in the Lanatoside Delayed series. In the latter, the average number of days is computed from the time the administration of the drug was begun. The control group of patients were not given digitalis at any time during their hospital stay. Reprinted from the AM. HEART J. 21: 138, 1941.

Ten of the thirteen patients with auricular fibrillation responded equally well to the intravenous administration of lanatoside C, whether the heart rate was 140 or 90 (Table II). Four had rates between 120 and 140; six had rates between 100 and 120; and two had rates between 90 and 100. One patient with an initial apical rate of 60 showed marked improvement following administration of the drug, as his case history illustrates:

O. W., a 63-year-old colored man with a history of hypertensive heart disease of six years' duration, was admitted complaining of increasing dyspnea, orthopnea, and edema of thirty days' duration. He stated that he had been taking 0.1 and 0.3 Gm. of folia digitalis on alternate days for a year. He appeared moderately dyspneic, orthopneic, and cyanotic, and râles were heard at both lung bases. His heart was enlarged; the rate was 60 beats per minute; and the rhythm was apparently regular. There was an apical systolic murmur. The blood pressure was 180/100; the liver was enlarged and tender; and there was a 2 plus pitting edema of both extremities. He was given 0.8 mg. of lanatoside C intravenously and responded within ten days with disappearance of the signs and symptoms of congestive heart failure. An electrocardiogram taken shortly before the drug was administered showed auricular fibrillation which had not been detected during physical examination. This patient manifested no signs of digitalis intoxication.

Except in this one instance, we did not give patients with auricular fibrillation and apical rates below 90 lanatoside C intravenously. We might have used the atropine sulfate test described by Gold and his co-workers[4] to aid in determining if such patients should be given lanatoside C. These investigators state that an acceleration of more than 15 to 20 beats per minute in the heart rate within fifteen to thirty minutes after the injection of 2 mg. of atropine sulfate indicates that the optimal dosage of digitalis has not been administered. The control of the heart rates of patients with auricular fibrillation on maintenance doses of digitalis is twofold. When the heart rate accelerates following atropine, this indicates that vagal stimulation is responsible for the slow heart rate. In the adequately digitalized patient with auricular fibrillation, the heart rate fails to increase following the injection of atropine because digitalis is acting not only upon the vagus but also upon the myocardium itself.

The five patients who are designated in the charts as having shown no improvement failed to evince persistent clearing of their heart failure after twenty-five to fifty days. All were then given diuretics in addition to digitalis. These patients were discharged, or deserted, with minimal but definite evidence of persistent decompensation although they were much improved. They were followed in the clinic and were advised to take 0.2 to 0.3 Gm. of folia digitalis daily. This enabled them to stay at home for long periods before their symptoms again forced them into the hospital. Most cardiologists are familiar with the problem presented by this type of patient who is never free of the signs and symptoms of congestive heart failure, but who, with a minimum of physical activity, can remain fairly comfortable at home while taking digitalis.

Of forty-four patients who had electrocardiograms taken before and after the administration of lanatoside C, twenty-four showed "digitalis effect" before the drug was given. The electrocardiographic evidence of digitalis was more pronounced in some instances after lanatoside C had been given, and the effect on the ventricular gradient of these patients is under study. The twenty other patients showed electrocardiographic effects only after receiving lanatoside C. At present it is our belief that electrocardiographic evidence of digitalis intake is not an index of maximal therapeutic dosage of the drug.

Only one of the sixty-two patients evidenced a toxic reaction to the intravenous administration of lanatoside C. This patient was a 64-year-old colored man who had taken digitalis intermittently for seventeen years. At the time of this admission, he gave a history of six weeks' progressive distress from dyspnea, orthopnea, and swelling of the legs and abdomen. He stated that he had been taking 0.1 Gm. of folia digitalis daily. He was dyspneic, orthopneic, and cyanotic, his neck veins were distended, and râles were heard at both lung bases. On the right, an area of dullness extending from the tenth to the sixth rib was noted. His heart was enlarged; the rate was 96; and the rhythm was regular. A systolic murmur was heard over the entire precordium; the pulmonic second sound was greater than the aortic second sound; and the blood pressure was 120/90. The liver was felt 8 cm. below the costal margin in the midclavicular line, and there was a 2 plus pitting edema of the extremities. His electrocardiogram showed left bundle branch block and evidence of digitalis effect.

He was given 1.2 mg. of lanatoside C and within thirty minutes developed nausea, emesis, blurred vision, extrasystoles, and pulsus bigeminus. He was then given 2 mg. of atropine sulfate intravenously in an attempt to counteract these effects,[5] and thirty-six hours later most of the toxic manifestations had disappeared.

It was later learned from the patient's wife that, instead of taking 0.1 Gm. of folia digitalis daily, as he had told us, he had in reality been getting 0.5 to 0.7 Gm. orally for seven days before his admission to the hospital, and had "lost weight" and "looked better" during that week. Had the true history been known, this toxic reaction would not have occurred, since no one would attempt intravenous digitalization of a patient already taking such large amounts of digitalis.

Of the sixty-two patients, eleven or 17.7 per cent died. This mortality is relatively small if compared with that previously observed[2] in a study of patients who were not taking digitalis when their heart failure occurred. In Table IV, from this previous study, it will be seen that, of fifty-two patients with regular sinus rhythm, 25.9 per cent died and, of sixty-seven patients with auricular fibrillation, 22.4 per cent died. All these patients had initial venous pressures above 15 cm. of water, as did the sixty-two patients currently reported.

Nine of the eleven patients died four to thirty days (average fourteen days) after the intravenous administration of lanatoside C, and it is unlikely that injection of the drug had any relation to the cause of death. Two patients died eighteen hours after intravenous administration of 0.8 mg. of lanatoside C; one of these had a cerebrovascular accident, the other expired in his sleep with no known pre-agonal episode. It is possible that the death of this patient might be ascribed in part to the administration of lanatoside C, but it is equally likely that it was unrelated to the drug.

DISCUSSION

The lack of toxic reactions and the definite evidence of improvement following the intravenous administration of lanatoside C to patients taking maintenance doses of folia digitalis before and during the development of congestive heart failure suggest several conclusions. Since the rate of improvement was more rapid than that to be expected from bed rest alone, it seems obvious that these patients were not receiving adequate therapeutic amounts of digitalis. A combination of factors may explain the tolerance of these patients to the intravenous administration of lanatoside C—the need for more digitalis when heart failure occurs, no matter what the precipitating cause, plus the possibility that the destruction and elimination of the digitalis accumulated during the previous period of "digitalization" contributed to the onset of congestive failure.

From our results, it would seem to be reasonably safe and usually of therapeutic benefit to give 0.4 to 0.8 mg. of lanatoside C intravenously to patients who develop congestive heart failure while taking maintenance doses of from 0.1 to 0.3 Gm. of folia digitalis.

Finally, this study indicates that the mere finding of "digitalis effect" in the electrocardiogram is apparently not proof that the patient is receiving adequate therapeutic doses of the drug.

CONCLUSIONS

1. The intravenous administration of from one-half to the full digitalizing dose of lanatoside C to patients developing congestive heart failure while taking maintenance doses of *Digitalis purpurea* was followed by definite improvement in forty-six of the sixty-two patients so treated.

2. Objective evidence of improvement was shown by thirty-six of forty-nine patients with regular sinus rhythm and by ten of thirteen patients with auricular fibrillation.

3. There was only one toxic reaction among the sixty-two patients.

4. The presence of electrocardiographic evidence of "digitalis effect" is not proof that therapeutic amounts of digitalis are present in the body.

5. The mortality of the patients studied was no greater than that previously observed in a group of patients with heart failure of comparable severity who had not been taking digitalis within three weeeks prior to intravenous digitalization.

6. None of the deaths occurring during this investigation could be attributed to the intravenous administration of lanatoside C.

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ADDENDUM

Since submission of this manuscript, thirty-five patients with regular sinus rhythm and fifteen patients with auricular fibrillation have been added to the series. There were no toxic manifestations in the patients with auricular fibrillation; six of the patients with regular sinus rhythm developed transient toxic reactions. Thus, of 104 patients with regular sinus rhythm, seven, or 6.7 per cent, developed nausea, emesis, and occasional extrasystoles. None of the patients with auricular fibrillation experienced toxic reactions, and no deaths could be attributed to the administration of the drug.

THE DIFFERENTIATION OF NORMAL FROM ABNORMAL Q WAVES

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ALTHOUGH analysis of each of the deflections of the QRS complex has always interested electrocardiographers, the criteria of Pardee and others[1, 2, 3] for the differentiation of normal from abnormal Q waves, and the importance of initial QRS deflections in the diagnosis of myocardial infarction[4] have served to stimulate search for the mechanisms responsible for both normal and abnormal Q waves. Part of the difficulties encountered in the study of the Q wave has centered around the definition of Q. As generally interpreted, the Q wave is an initial downward deflection, followed by an upward deflection, in any lead. However, in many cases, especially in Lead III, a small, and sometimes insignificant, upward deflection can be found preceding the main downward deflection. Many observers have ignored this initial upward deflection in their studies and have called the main downstroke Q.

For the purposes of this paper, the Q wave shall be defined as an initial downstroke. If this deflection is preceded by an upstroke, no matter how small, so long as it is visible with the naked eye, this initial upstroke is an R wave and the downstroke which follows is an S deflection. If the QRS complex consists only of a downstroke, this may be labeled a QS wave, but we shall analyze it in the same manner as the ordinary Q wave.

Another difficulty which is encountered in study of the Q wave lies in the fact that the initial downstroke may be produced by many factors. In the standard leads, which record the difference between the potentials at two extremities, the record is taken in such a manner that when the initial potential of the right arm is relatively positive to the initial potentials at the left arm and left leg, the initial deflections in Leads I and II will be downward. This initial downstroke is, of course, a Q wave. In Lead III, a Q deflection is produced when the initial potential at the left arm is relatively positive to the initial potential at the left leg. Since this is so, a Q wave in any of the standard leads may be produced by five different combinations of potential at the two extremities. For example, Q_3 may be produced by: (1) An initial negative potential at the left leg and an initial positive potential at the left arm, (2) An initial negative potential at the left leg and an initial zero potential at the left arm, (3) An initial zero potential at the left leg and an initial positive potential at the left arm, (4) An initial positive potential at the left leg and an initial positive potential at the left arm (in such a case the left arm potential is more positive than that at the left leg), and (5) An initial negative potential at the left leg and an initial negative potential at the left arm (in such a case the left arm potential is less negative than that at the left leg). On theoretical analysis, therefore, we reach the interesting conclusion that a Q wave in a standard lead may occur *even if the initial potentials at both extremities are positive.*

It therefore becomes obvious that study of the Q wave by means of standard leads leaves much to be desired. Fortunately we are not limited to the

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use of standard leads alone, nor to theoretical analysis of the potentials at each of the extremities, because, with a very simple technique, the actual unipolar extremity potentials can be recorded,[5] and the mechanisms which produce Q waves can be more exactly studied. Fig. 1, for example, illustrates two variations in unipolar extremity lead potentials which can produce a Q_3 deflection. In Fig. 1, *a*, the Q_3 wave occurs because of an initial negative deflection in the left leg lead and an initial positive deflection in the left arm lead. However, in Fig. 1, *b*, although a Q_3 deflection is present, the initial potentials at both the left arm and left leg leads are actually positive. Because this is so, it would appear that study of the Q wave resolves itself into two problems at least: (1) an analysis of the actual potentials at each extremity which cause the various Q-wave patterns, and (2) an attempt to define the Q wave, if possible, in terms of the spread of the initial activity within the heart. We have used both these approaches in the following report.

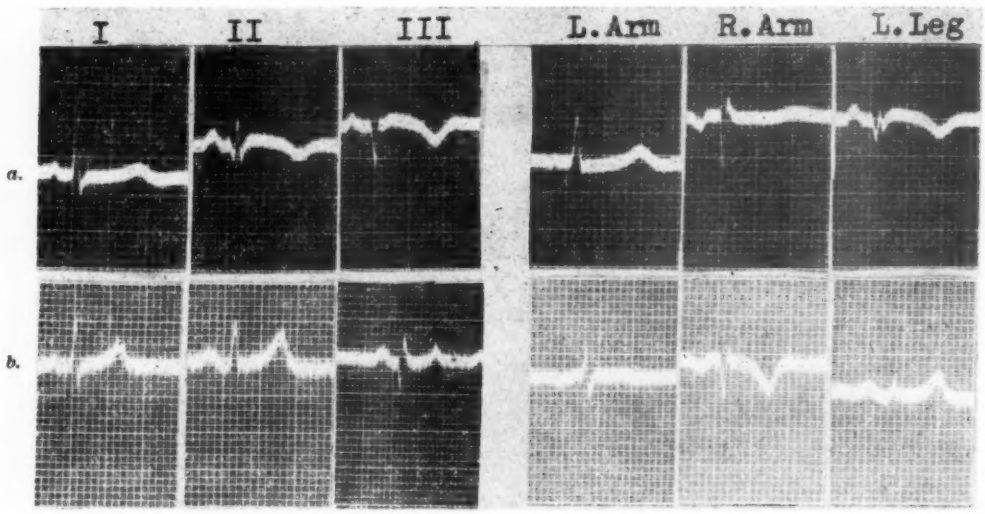


Fig. 1.—Two different mechanisms which can produce a Q_3 wave. *a*, A case of posterior infarction; N. L., male, 61 years of age. *b*, A normal heart; J. B., male, 65 years of age. *L.Arm*, *R.Arm*, and *L.Leg* represent unipolar extremity leads taken with the author's technique.[5]

MATERIAL AND TECHNIQUE

For this paper I reviewed the electrocardiograms of more than five hundred cases from our files. These included the records of two hundred normal subjects and patients with normal-sized hearts; two hundred patients with cardiac hypertrophy (thickening of the right or left ventricle, or both); one hundred cases of myocardial infarction; and fifty cases of bundle branch block. In most of these cases, multiple unipolar precordial leads had been taken in addition to the unipolar extremity leads and standard leads. The unipolar leads were taken with the author's indifferent electrode of zero potential,[5] and the author's technique of obtaining augmented unipolar extremity leads was used.[5] In addition to this, multiple unipolar leads from twenty or more points on the surface of the body were taken in seventy-five of the cases.

METHOD AND RESULTS

Although it is possible, as I pointed out, for a Q wave to appear in a standard lead, even if the initial potentials at both extremities are positive, I found as a general rule that: (a) Q_1 was usually associated with a Q wave

in the left arm lead (Q-LA), especially if a Q wave was absent in Lead III, and (b) Q_3 was usually associated with a Q wave in the left leg lead (Q-LL), especially if a Q_2 was also present. Exceptions to these rules will be found throughout the paper.

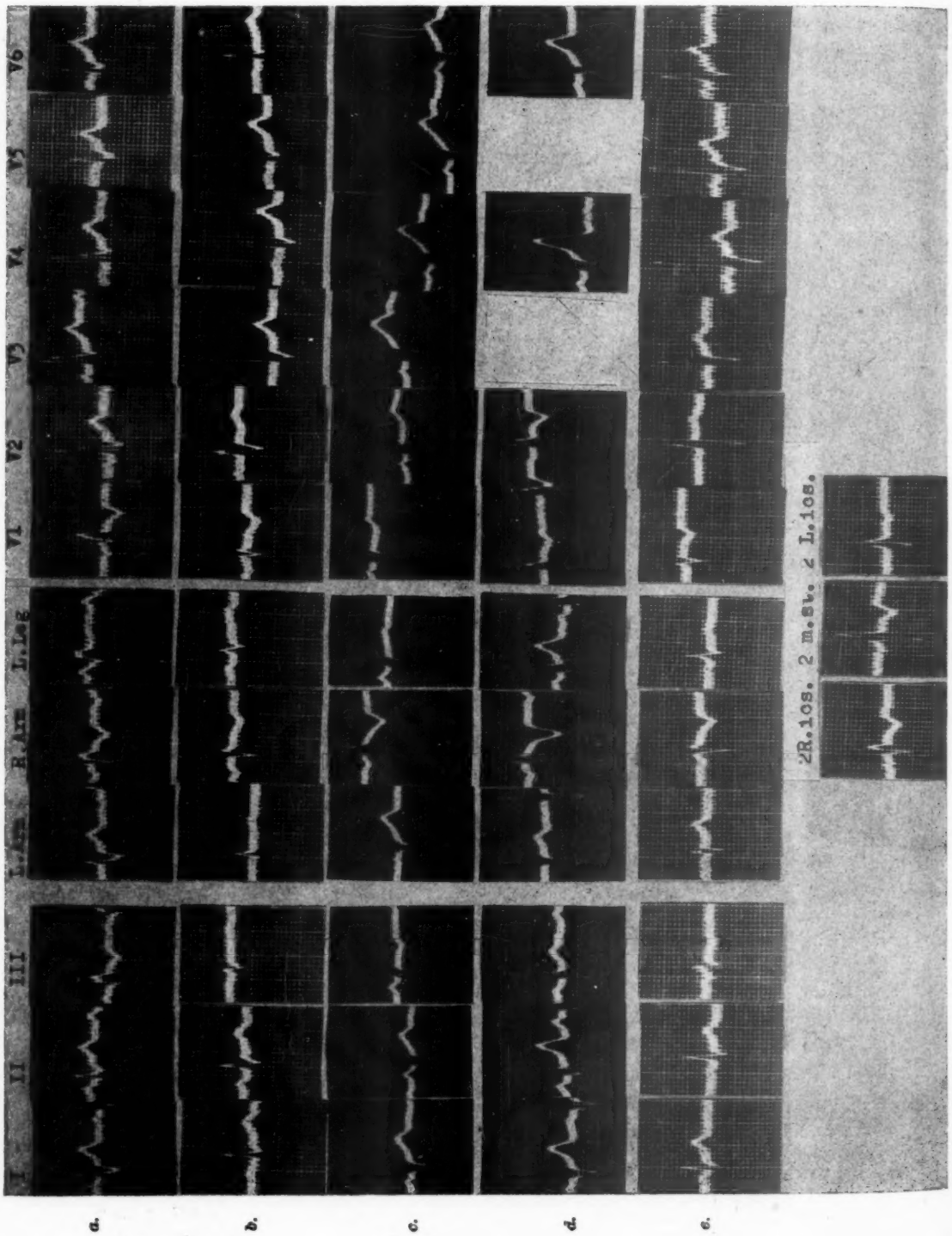
In my study of the origin of the Q wave I used a method of analyzing the QRS complex in terms of the spread of the impulse through the ventricles which depends on the following physiologic principles, which are valid when the electrical activity of the heart is studied with unipolar leads:[6, 7] (1) An electrode facing a region to which the electrical activity is spreading will record a positive deflection. (2) An electrode facing this same region, but in the direction from which the impulse is passing, will record a negative deflection. (3) If the impulse runs at right angles to an axis formed by drawing a line from the electrode to the region of electrical activity, the electrode will not record the electrical activity.[8, 9] (4) Within the ventricles, the electrical activity spreads from the subendocardial region outward to the epicardium of both ventricles, so that the endocardium tends to be negative throughout the entire QRS complex.[10, 11] Statement 4 does not take into account the electrical activity of the interventricular septum because it has been assumed in the past that the impulse also spreads from the endocardium on both sides of the septum inward, thereby nullifying the electrical effects of the septum.[12]

We believe, however, that the left side of the interventricular septum is activated earlier than the right side and that the spread of the impulse through the septum from left to right is the basic cause of the Q wave in the human electrocardiogram. The following observations support such a concept:

The Relationship Between the Normal Electrocardiogram and the Patterns of Right Bundle Branch Block.—

A. Even if we assume the problem of septal activation in the normal heart to be unanswered, no one can question the fact that in cases of right bundle branch block the left side of the septum is activated earlier than the right side. Therefore a unipolar lead placed on the chest in such a position that it faces the right side of the septum will record this initial septal activity with an initial positive deflection. Similarly, a unipolar lead taken from a point on the chest facing the left side of the septum will record this initial septal activity with an initial negative deflection (Fig. 2,*a*). In addition to these initial deflections, the precordial leads in cases of right bundle branch block have the following characteristics:[7] (a) Precordial leads near the sternum, which face the right side of the septum, have an M-shaped QRS complex. (b) Precordial leads which face the left side of the septum have a W-shaped QRS complex, although the initial Q wave is often small and inconspicuous. (c) Although bundle branch block is usually not considered to be present until the QRS interval exceeds 0.12 second, it is well known that cases of right bundle branch block may have a QRS interval which does not exceed 0.1 second.[12] In my series of records from normal subjects or from patients without heart disease (determined on the basis of history, physical examination, and x-ray study) I found ten cases in which the precordial leads were very similar to the patterns found in right bundle branch block. Four of these cases are illustrated in Fig. 2. An M-shaped QRS complex is present in precordial Lead V_1 (Fig. 2,*b*), and in Leads V_1 and V_2 (Fig. 2,*c* and *d*). A W-shaped QRS complex is present in precordial Leads V_3, V_4, V_5, and V_6 (Fig. 2,*b*); Leads V_5 and V_6 (Fig. 2,*c*); and Lead V_6 (Fig. 2,*d*). The patterns in the standard and unipolar extremity leads can be correlated with these precordial lead patterns if one remembers that, when the heart is horizontal, the left arm lead and Lead I tend to resemble leads facing the surface

of the left ventricle; and when the heart is vertical, the left leg lead and Leads II and III tend to resemble the precordial leads facing the left ventricle.[6] Therefore, in Figs. 2,*b*, *c*, and *d*, the left arm lead and Lead I have a Q deflection. In Fig. 2,*d*, the left leg is also facing the left ventricle, and the left leg lead and Leads II and III also have Q waves. Although an M-shaped QRS complex in



the first two precordial leads is not ordinarily seen in the normal electrocardiogram, nevertheless in cases where the first two precordial leads show the usual pattern, the M-shaped QRS complex can often be seen in unipolar leads taken higher on the anterior chest wall, such as over the sternum at the level of the second intercostal space, Fig. 2,*e*, shows such a record.

B. The histological studies of Mahaim[13] support such a concept, as does recent interpretation of the standard leads on the basis of vector analysis.[14]

C. Experimental records obtained from within the ventricular cavity of dogs often exhibit a small upward deflection preceding the main negative deflection when the electrode is placed within the right ventricular cavity, and it was suggested some years ago that this small upward deflection might be due to early activation of the left side of the septum in advance of the right side.[11]

D. A small R wave is found in human beings in precordial leads close to the sternum,* whereas in one or more of the precordial leads over the left side of the chest a small Q wave may usually be observed.

E. Finally, we may point out that a Q wave and an S wave, such as Fig. 2,*c*, shows, in the standard leads is considered one of the basic characteristics of the normal standard lead electrocardiogram.

We may therefore conclude that in a normal heart, at least, a Q wave in a unipolar lead is due to the fact that the left side of the interventricular septum is the first region of the heart to be activated. It should, however, be remembered, as I emphasized in the introduction, that if an electrode lies on the same plane as the septum, for example, the initial impulse which is passing at right angles to this plane will not be recorded by the electrode so placed. Consequently not every initial impulse, either positive or negative, even if recorded by unipolar leads, can be said to be due to septal activity. Therefore with the exception of this condition, a Q wave should be found in all unipolar leads which face the left side of the septum, and an initial positive deflection should be found in those unipolar leads which face the right side of the septum.

To theorize further, two types of unipolar leads with a Q wave can be anticipated: (1) Leads facing the endocardium of the left ventricle and the left side of the septum should display not only a Q wave but a downward main QRS deflection. Thus, the QRS complex might consist of a QS deflection. (2) Leads facing the left side of the septum and the epicardial surface of the left ventricle should display an initial Q wave due to septal activity, followed by a high R wave due to the spread of the impulse outward through the left ventricular wall. In an attempt to confirm this concept I studied the initial deflections in a series of seventy-five cases in each of which twenty or more unipolar leads had been taken from the surface of the body.

Before discussing the results, however, it should be emphasized that in all studies on the distribution of potentials from the surface of the heart to

*We do not wish to imply by this statement that the entire deflection of such an initial R wave is due to septal activity, because part of it is due to the wave of activation passing outward through the free wall of the right ventricle.[12]

Fig. 2.—Cases illustrating the relations between normal electrocardiograms and the pattern of right bundle branch block. *a*, right bundle branch block; R. B., female, 67 years of age. *b*, Normal heart; E. P., female, 73 years of age. *c*, Normal heart; I. H., male, 19 years of age. *d*, Normal heart; H. R., male, 12 years of age. *e*, Normal heart; P. S., female, 22 years of age. V_1 to V_6 represent unipolar precordial leads. The electrode was placed in the following positions: V_1, fourth intercostal space to right of sternum; V_2, fourth intercostal space to left of sternum; V_3, midway on a line joining points of V_2 and V_4, fifth intercostal space on left mid-clavicular line; V_5, continuation of fifth intercostal space on left anterior axillary line; V_6, continuation of fifth intercostal space on left midaxillary line. Three other unipolar leads are shown in *e*: *2R.ics.*, electrode on second right intercostal space on mid-clavicular line; *2m.st.*, electrode over sternum at level of second intercostal space; *2L.ics.*, electrode on second left intercostal space on mid-clavicular line.

the surface of the body, variations in the position of the heart within the thorax are accompanied by marked variations in the distribution of the potentials on the surface of the body and the extremities. The effect of a horizontal or vertical heart on the extremity patterns has already been mentioned briefly. This can now be further discussed. The position of the heart may vary because of rotation around any one or more of the following three axes: (A) Rotation around an anteroposterior axis. This causes the long axis of the heart to become horizontal or vertical. (B) Rotation around the long axis of the heart. This causes the right ventricle to move anteriorly, or to the right. (C) Rotation around a transverse axis. This causes the apex of the heart to be pushed forward or backward. Although a detailed description of the effects of rotation on the distribution of potentials over the surface of the body will not be given, the effects of such rotations on the extremity leads can be briefly sketched, although it must be remembered that countless variations may exist, determined not only by the position of the heart, but also by the size and shape of the thorax, and other factors.

1. When the heart lies vertically, it is usually also rotated clockwise around its long axis and the following occurs: (a) The left arm lead tends to face the endocardium of the heart and the right side of the interventricular septum. Its initial deflection should be upward, followed by an S. (b) The right arm lead tends to face the endocardium of the heart and the right side of the septum. Its initial deflection therefore also should be upward, followed by an S. (c) The left leg lead faces the left side of the septum and the epicardial surface of the left ventricle. A Q wave followed by a high R wave should occur. A heart in such a position should cause the pattern in the standard leads, described as right axis deviation, with Q_2 and Q_3 waves. If the clockwise rotation around the long axis becomes marked, the right arm lead may lie on the same plane as the septum or actually face the left side of the septum, and the initial deflection will be downward.

2. When the heart is horizontal, it is usually rotated counterclockwise around its long axis, and the following should occur: (a) The left arm lead now faces the left side of the septum and the epicardial surface of the left ventricle. A Q wave followed by a high R wave should be present. (b) The right arm lead continues to face the right side of the septum and the endocardium. Its initial deflection should be upward, followed by an S wave. (c) The left leg lead faces the right side of the septum and the epicardial surface of the right ventricle. Its initial deflection should be upward, followed by an S wave.*

3. When the apex is pushed forward, the following occurs: (a) The left arm lead tends to resemble potentials from the anterior surface of the ventricles. The initial deflection will vary, depending on whether the left arm is facing more of the right ventricle than the left, and on other factors. (b) The right arm lead tends to be similar to unipolar precordial leads near the sternum. The initial deflection will be upward followed by a deep S wave. (c) The left leg lead tends to record potentials from the epicardial surface of the left ventricle. A Q wave followed by an R deflection should occur.

4. When the apex of the heart is pushed backward, the following occurs: (a) The left arm lead tends to resemble unipolar leads, ordinarily derived from the left upper back. In such leads (on the basis of my observations) the

*The S wave is due to the fact that the right ventricle is smaller than the left ventricle. Thus, the potentials developed within it are weaker than those developed by the left ventricle, and an electrode, although facing the epicardial surface of the right ventricle, is also facing the tail of the wave passing outward through the left ventricle, causing the main deflection to be downward.

Q wave is usually deep and the R deflection is of variable size. (b) The right arm lead also tends to resemble unipolar leads ordinarily obtained from the right upper back. Such leads often have a deep Q wave followed by a high R deflection. (c) The left leg lead tends to resemble potentials from the epicardial surface of the right ventricle. The initial deflection should be upward followed by an S wave.

With these facts in mind, the results can now be analyzed. Fig. 3 illustrates the distribution of potential over the surface of the body in a normal subject. This record and Fig. 2,*d*, are from the same patient. A small Q wave, followed by a high R deflection, can be seen in both the left arm and left leg leads (Fig. 2,*d*), showing that the position of the heart is neither fully vertical nor fully horizontal. Consequently the regions of the surface of the body facing the left ventricle are extensive and unipolar leads (Fig. 3) from the left upper chest (*2 L.ics.*), the abdominal wall (*RUA* and *LUA*), and lower back (*l.B.*) show a Q deflection and high R wave. A small R deflection followed by a deep S wave is found, on the other hand, in unipolar leads from the right upper chest wall. The unipolar leads from the back in this case illustrate particularly well the transition of the two types of Q-wave patterns described above. The upper scapular lead (*u.Sc.*) is completely negative. At the level of the scapular angles

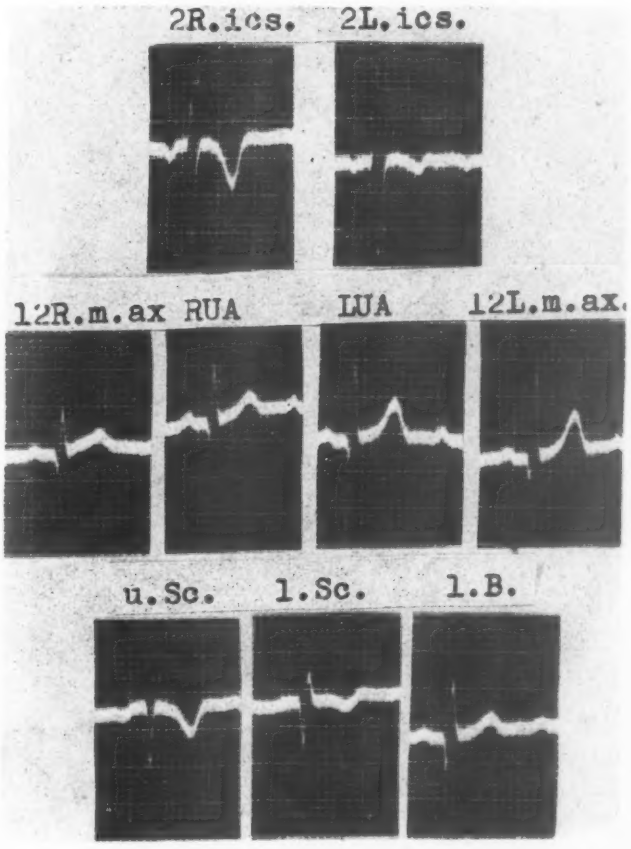


Fig. 3.—Unipolar leads in a normal subject. The standard, unipolar extremity, and precordial leads of this subject are illustrated in Fig. 2,*a*. The other unipolar leads shown are: *12R.m.ax.*, electrode on right midaxillary line at level of twelfth intercostal space; *RUA*, electrode on continuation of right mid-clavicular line at level of lowest border of ribs; *LUA*, like *RUA*, but on left side; *12L.m.ax.*, like *12R.m.ax.*, but on left side; *2R.ics.*, electrode on second right intercostal space on mid-clavicular line; *2L.ics.*, like *2R.ics.*, but on left side; *u.Sc.*, electrode on back at level of base of spines of scapulae, just to the left of the midline; *l.Sc.*, electrode on back at level of angles of scapulae, just to the left of the midline; *l.B.*, electrode on the back at level of twelfth rib, just to the left of the midline.

it is biphasic and consists of a deep Q wave and high R deflection (*l.Sc.*). The T wave is still negative here. At the level of the lower back (*l.B.*), although the Q wave is still deep, the R deflection has become tall and the T wave has become positive. This pattern is similar to the left leg lead and Lead III. This case also illustrates another important characteristic of the Q waves obtained from different portions of the body. When the Q is recorded by a lead which faces the epicardial surface of the left ventricle, its duration* is shorter than in those leads facing the endocardium of the left ventricle. In this case, as in the other cases with a normal QRS interval in the series, the duration of the Q wave in the back leads was 0.04 to 0.06 second. This approximates the entire duration of the QRS complex. However, in the leads facing the epicardial surface of the left ventricle, the duration of the Q wave was less than 0.04 second. This will be further discussed in a later section of the paper.

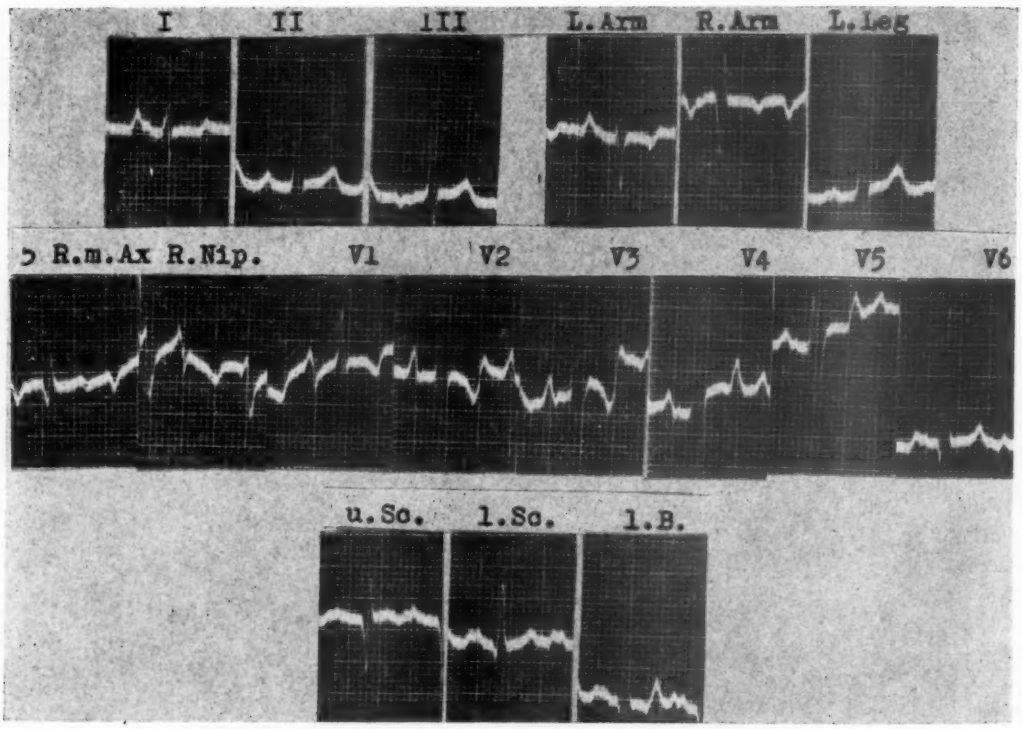


Fig. 4.—A vertical heart with right axis deviation but without Q_2 and Q_3. A case of mitral stenosis and insufficiency; G. M., male, 12 years of age. The patient had been digitalized. *5R.m.Ax.*, electrode on right midaxillary line at level of fifth intercostal space; *R.Nip.*, electrode over right nipple. For explanation of the other leads, see captions of Figs. 3 and 4.

THE Q WAVES IN CASES IN WHICH THE HEART IS VERTICAL

If, as we have stated, right axis deviation is due to a vertical heart, the left ventricle will face the left leg, and the left leg lead and Leads II and III should have a Q wave. We studied one hundred forty cases showing right axis deviation with this in mind. These cases included patients with normal-sized hearts, and patients with left ventricular hypertrophy as well as those with right ventricular hypertrophy. A Q wave was found in one hundred thirty cases in the left leg lead, in Lead III, and, in most of the cases, in Lead II. In only ten cases was a Q wave absent in the left leg lead and Leads II and III. Careful unipolar lead studies were made in six of these ten cases, and

*The duration of the Q wave is the interval between its downstroke and upstroke. It is measured at the upper level of the string image.

in all of them were found a Q wave and a high R deflection, either posteriorly over the lower back, or in the left axilla. This, in itself, indicates that the position of the heart in such cases is different from that which occurs in the ordinary cases of right axis deviation.

Fig. 4 illustrates why a $Q_{2,3}$ is absent in such cases. This is the record of a 12-year-old boy with rheumatic heart disease and mitral stenosis. He was in congestive heart failure and was receiving digitalis. Although right axis deviation is present, there is no Q wave in either the left leg lead or Leads II and III, although a small Q wave with a high R deflection can be seen in precordial Lead V_6, and in all the unipolar leads taken from the back. The reason for this becomes clear if we study the right arm lead. A deep Q deflection with a high R wave is present. This, as was previously mentioned, is an indication

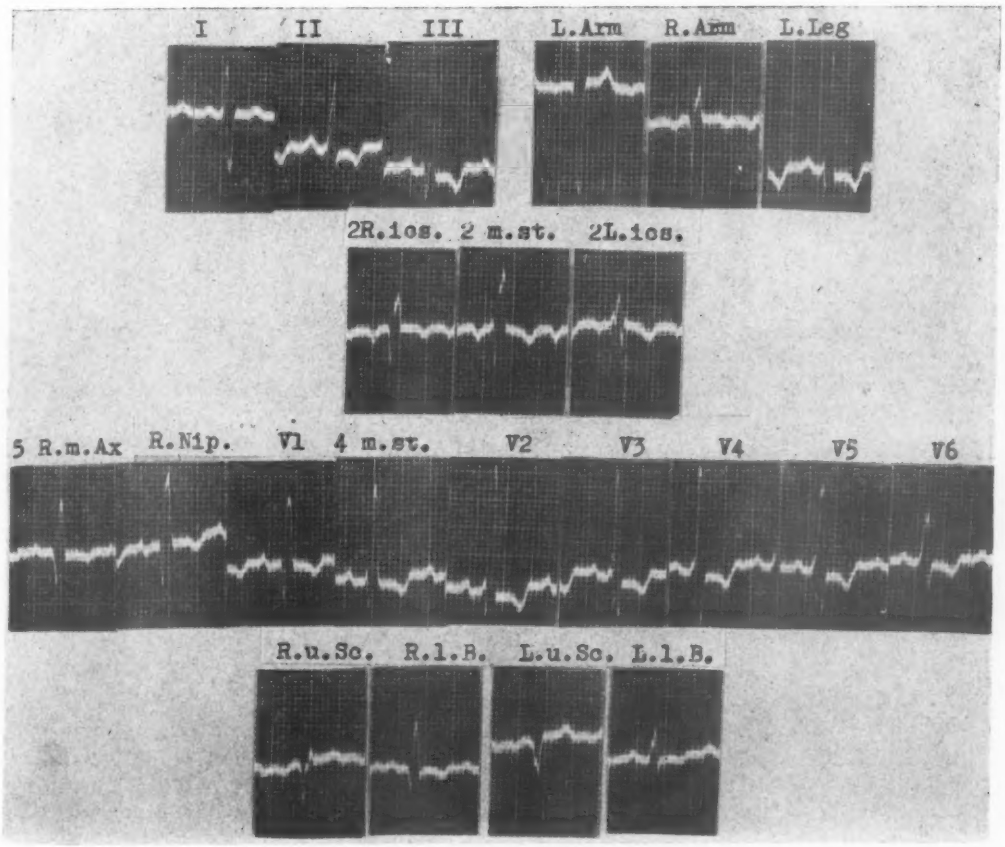


Fig. 5.—A vertical heart with right axis deviation but without a Q_2 and Q_3. A case of interauricular septal defect; J. D., female, 36 years of age. Patient was receiving no medication. *4m.st.*, electrode over sternum at level of fourth intercostal space. *R. and L.u.Sc.*, electrodes at bases of spines of scapulae. For explanation of the other leads, see captions of Figs. 3 and 4. *R.* and *L.l.B.*, electrodes on back in twelfth intercostal space directly under the angles of the scapulae.

that the apex of the heart has been pushed backward. In such a case, in spite of the right axis deviation and vertical position of the heart, the left leg lead will tend to face the right ventricle instead of the left ventricle. Therefore, no Q waves should be expected in the left leg lead or Leads II and III. The high amplitudes of the R waves in these leads, in this case, are due to the right ventricular hypertrophy which was present.

There is another type of Q wave which occurs occasionally in cases of right ventricular hypertrophy. This occurs with a high R deflection and is

found in precordial leads near the sternum. Although the precordial leads of Fig. 4 did not show this, Fig. 5 illustrates a case of right ventricular hypertrophy in which a Q did occur in precordial Lead V_1. This was the record of a 36-year-old woman with an interauricular septal defect. She was not receiving any medication. In this case, the unipolar leads which were taken across the chest illustrate well the development of the small initial upward deflection ordinarily noted, and the origin of the Q wave. Precordial Lead V_1 begins with a deep Q deflection. This is similar to unipolar leads from points over the right nipple (*R. Nip.*); the right midaxillary line in the fifth intercostal space (*5R. m.Ax*); the second right intercostal space on the mid-clavicular line (*2R.ics.*); and the right arm lead. However, a precordial lead over the midsternum at the level of the fourth intercostal space (*4 m.st.*) has a small initial upward deflection. This can also be observed in precordial Leads V_2, V_3, V_4, and even V_5, where it appears as a slurring on the large main upstroke of the QRS complex. Similarly, although a unipolar lead from the second right intercostal space on the mid-clavicular line (*2R.ics.*) has a Q wave, the unipolar lead overlying the sternum at this level (*2 m.st.*) has a characteristic initial upstroke. When this record is compared to Fig. 4 and Fig. 3 (which is from a normal subject), the Q wave in Fig. 4 was found only in the right arm lead and the right midaxillary lead (*5R.m.Ax*); and in Fig 3, a deep Q deflection was found only in the right arm lead and in the region of the midback.

On the basis of these observations and our detailed study of twenty similar cases of right ventricular hypertrophy,[15] we can describe the origin of the Q wave in such cases. With right ventricular hypertrophy, the position of the heart is usually vertical, and clockwise rotation of the heart around its long axis ordinarily occurs. If this clockwise rotation becomes marked, or if the large right ventricle displaces the position of the interventricular septum sufficiently, potentials which ordinarily would be projected to the right midback or the right midaxillary line, are projected anteriorly and a Q wave (which ordinarily is found in such regions) results. The Q deflection is therefore due to the fact that the electrode is either lying on the same plane as the interventricular septum or is actually facing the left side of the septum, because of the marked rotation, or displacement of the septum. The final R wave may be due to the passage of the impulse outward through either the right or left ventricular wall or through both. The Q in the right arm lead is due either to the marked clockwise rotation of the heart around its long axis, or to backward displacement of the apex, as was previously mentioned, or to a combination of both factors. Further proof that backward displacement of the apex has occurred can also be found in the standard and unipolar extremity leads in Fig. 5. Careful examination of Lead III and the left leg lead show that the initial deflection is not a Q wave but is upward, in spite of the fact that right axis deviation exists. Comparison of the left leg lead with the precordial leads indicates the marked similarity between it and precordial Lead V_2. This occurs, as has already been stated, when the apex of the heart has been displaced backward, so that the left leg lead records a pattern which can be found in precordial leads overlying the right ventricle, rather than the left ventricle.

Occasionally in cases of right ventricular hypertrophy a deep Q_1 occurs. There was one such case in the series. It is illustrated in Fig. 6. This is the record of a 36-year-old man with mitral stenosis, massive enlargement of the left auricle, and marked pleural effusion. Examination of Fig. 6 reveals the similarity between the right arm lead and unipolar leads from the right upper

chest (*2R.ics.*) and precordial leads near the sternum. All these leads have an initial R wave. On the other hand, precordial Leads V_5 and V_6, the left upper abdominal lead (not shown), the left leg lead, and the back leads have a small Q wave. The significance of the deep Q deflection in the left arm lead (and in Lead I) can be appreciated by comparing the left arm pattern with the record obtained from the second left intercostal space on the mid-clavicular line (*2L.ics.*). The two leads are similar except that the small R deflection present in the second left intercostal space disappears in the left arm lead. This can be explained by the fact that the left arm lead lies on the same plane as the interventricular septum. From the distribution of potentials in this case and the similarity of the right arm lead to the right anterior chest potentials, rather than to potentials from the back, and the similarity of the left leg lead to the precordial Lead V_6, we can assume that the apex in this case has been pushed forward. This is unusual in cases of right ventricular hypertrophy.

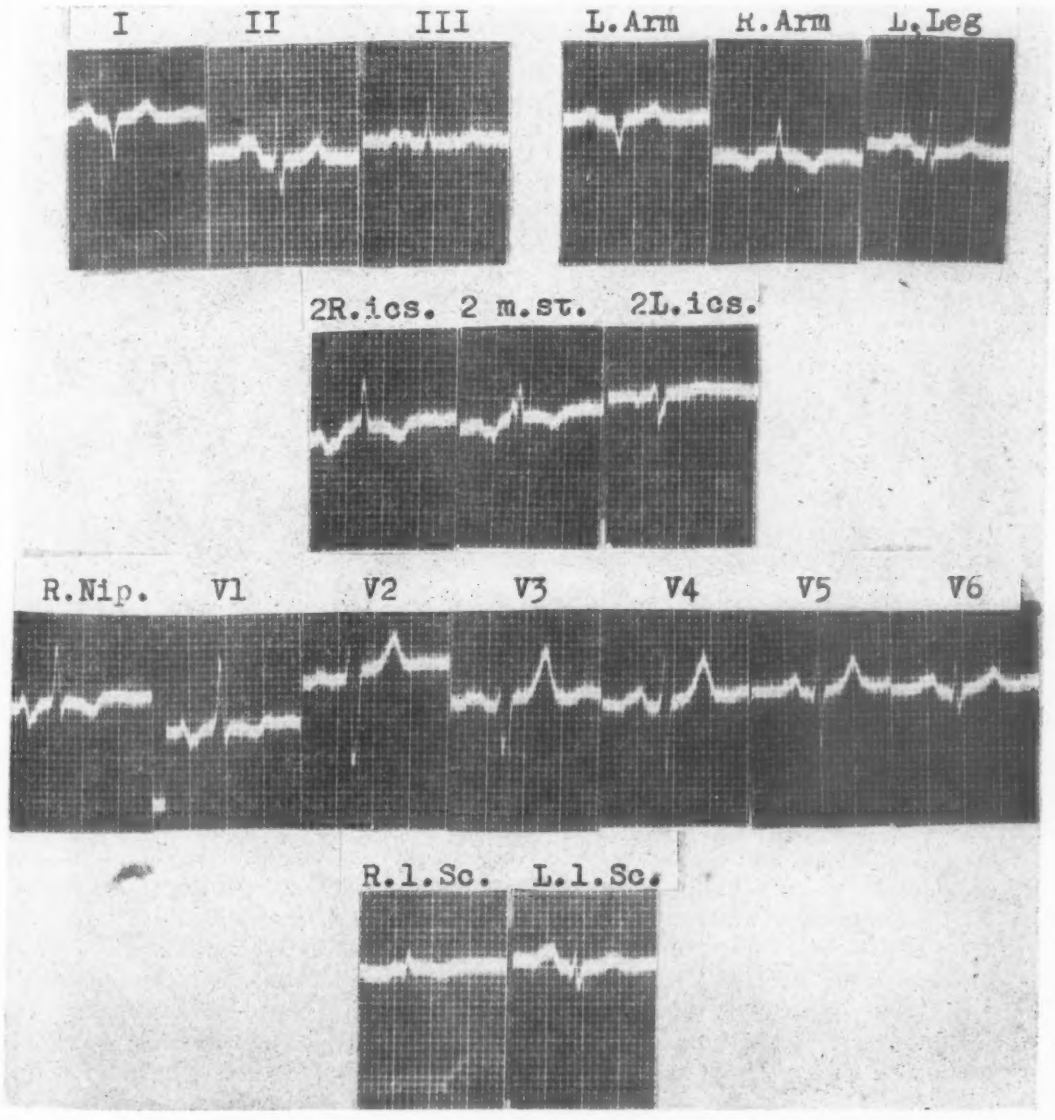


Fig. 6.—A vertical heart with a deep QS_1. A case of mitral stenosis. H. B., 36 years of age. Patient had been digitalized. For explanation of the leads, see captions of Figs. 3, 4, and 5.

THE Q WAVE IN CASES IN WHICH THE HEART LIES HORIZONTALLY

If, as I have stated, left axis deviation is due to a horizontal heart, the left ventricle faces the left arm lead and the left arm lead and Lead I should have a Q wave, and a high R deflection. A series of one hundred twenty cases showing left axis deviation in the standard leads were studied. These included persons with normal hearts, patients with enlargement of the left ventricle, and patients with enlargement of both the right and left ventricles. In one hundred seven cases, a Q_1 wave and a Q deflection in the left arm lead were found. In eight other cases, although a Q_1 wave was absent, a Q deflection was present in the left arm lead (Fig. 7,*a*). In five cases, although the pattern in the standard leads was that of left axis deviation, a Q wave was absent in Lead I and the left arm lead, but a Q deflection was found in the left leg lead (Fig. 7,*b*). Such cases had a very deep Q_3 deflection. Although we have not made sufficient studies in such cases to accurately describe the position of these hearts, it would appear that some degree of unusual rotation has occurred.

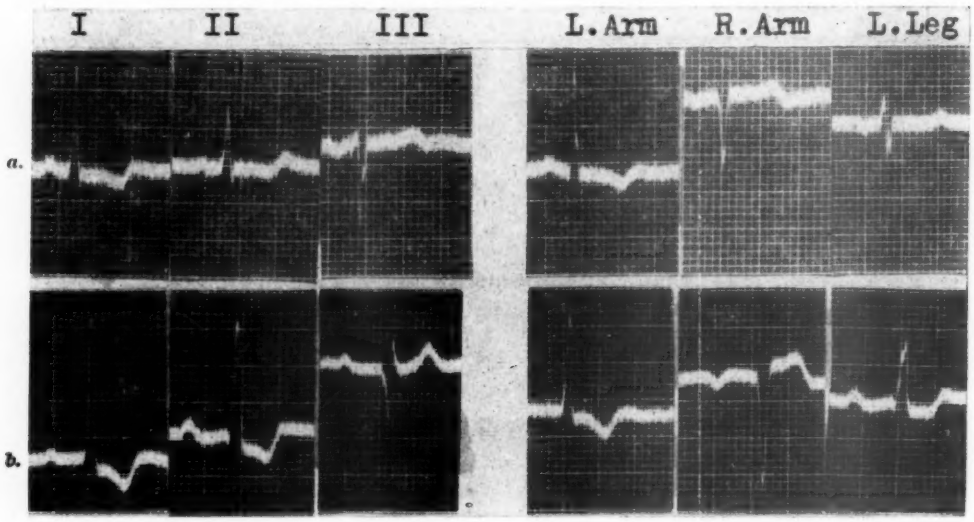


Fig. 7.—Two cases with horizontal hearts. For explanation see text.

THE Q WAVE IN CASES OF MYOCARDIAL INFARCTION

If the Q wave is due to early activation of the left side of the septum, variations in the distribution of the Q wave which are due to the position of the heart should be found in cases of myocardial infarction in a manner similar to that which occurs in the normal and hypertrophied heart. There is, however, another mechanism by which Q waves may occur after infarction. Such Q waves are deep, and the entire QRS complex may consist of a QS deflection. Such Q waves are found when the infarct tends to involve the entire thickness of the ventricular wall; they are recorded by unipolar leads which overlie or face the infarct. The explanation which has been advanced for the presence of these deep Q waves is that the large area of infarcted tissue is without electrical activity and acts like a window in the ventricular wall so that an electrode, overlying the infarct, records potentials similar to an electrode which would be placed within the ventricular cavity. Such Q waves we have noted also have an increased duration, similar to the Q waves which are normally recorded from leads facing the ventricular cavity. This concept, of course, assumes that the ventricular cavity is negative at the beginning of the QRS

complex. However, if, as I have stated, the left side of the septum is activated before the right side in a case with normal conduction or with right bundle branch block, only the cavity of the left ventricle will be negative when the QRS begins. Therefore, even if an electrode were placed over an extensive infarct of the right ventricular wall, Q waves should not be recorded from such leads. If the infarct is small, the initial deflections of the QRS complex, before and after the infarction, remain more or less unchanged, and deep Q waves do not develop.[16] Irrespective of whether Q waves are, or are not, present in a case of infarction, the most characteristic sign of an acute infarct is the presence of an elevation of the RS-T segment, fusing with the T wave, which is coved. This pattern is also found in unipolar leads which overlie, or face, the infarct.

We can, therefore, summarize the Q-wave patterns which may be anticipated in a case of myocardial infarction, in the following way: (1) With infarction of the right ventricle or of a region which is near the plane of the interventricular septum, a unipolar lead overlying the infarct will record RS-T elevation without a Q wave, even though the size of the infarct may be extensive. (2) With infarction of the anterior surface of the left ventricle, a unipolar lead overlying the infarct may record the characteristic RS-T elevation due to the infarct and a small Q wave, which is a normal phenomenon. (3) Infarction of the anterior or anterolateral surface of the left ventricle, involving a large part of the thickness of the muscle wall, should produce a characteristic deep Q wave followed by marked RS-T elevations in unipolar leads overlying the infarct. (4) If only the subendocardial layers of muscle are infarcted and the outer layer is normal, a unipolar lead overlying the infarct will record a fairly deep Q wave followed by an R or even an S deflection.[12] (5) Assuming that the infarct does not involve the entire surface of the left ventricle, regions should be found overlying normal muscle, in which a small normal Q wave may be recorded with a high R deflection and an upright or high T deflection (or with depression of the RS-T segment). (6) The patterns in the unipolar extremity and standard leads after infarction should depend on the position of the heart, just as in cases where the heart is normal or hypertrophied, as well as on the actual location and extent of the infarct. In other words, in a case of antero-lateral infarction of the left ventricle in a horizontal heart, the left arm lead and Lead I, which face this region, should show the characteristic Q wave and elevated RS-T complex; whereas if the heart were vertical, the left leg lead and Leads II and III, which now would face the infarcted region, should possess the characteristic Q wave and the elevated RS-T complex, in spite of the fact that the infarct was anterior. Similarly, in a case of posterior infarction, if the heart were vertical, the characteristic Q wave and elevated RS-T complex would be seen in the left leg lead and Leads II and III; whereas if the heart were horizontal, the left arm lead and Lead I would face the infarct and record a Q wave and elevated RS-T complex.

Before continuing the discussion, consideration should be given to the position of the heart in cases of infarction. I do not believe that a vertical or horizontal, normal or hypertrophied, heart occupies the same position as a vertical or horizontal heart in which infarction has occurred, because certain factors contribute to the changes in position after infarction which are different from those affecting a normal or hypertrophied heart. In the first place, a large area of muscle is no longer functioning normally, and the force of contraction of the remaining normal musculature may cause abnormal torsion of

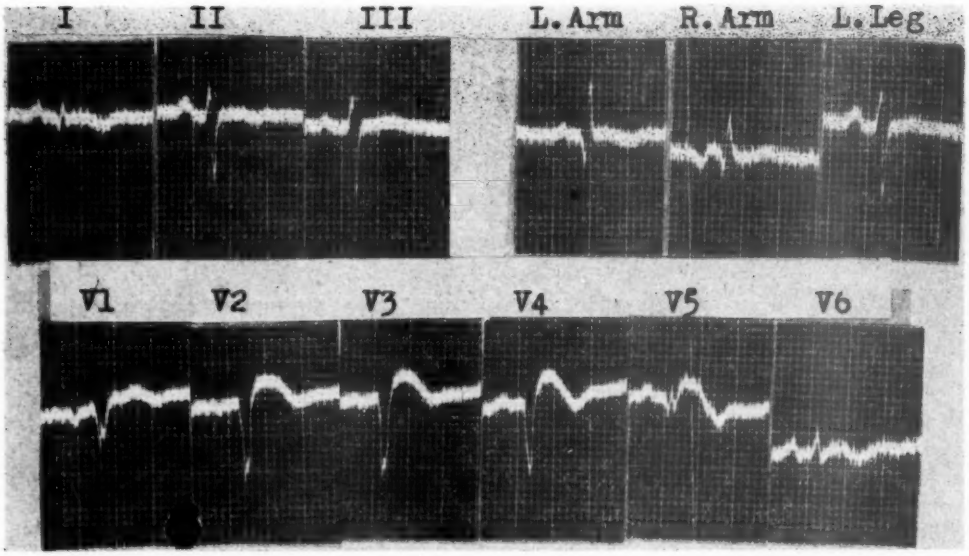


Fig. 8.—A case of anterior infarction with the heart in a horizontal position. A. F., a man, 69 years of age.

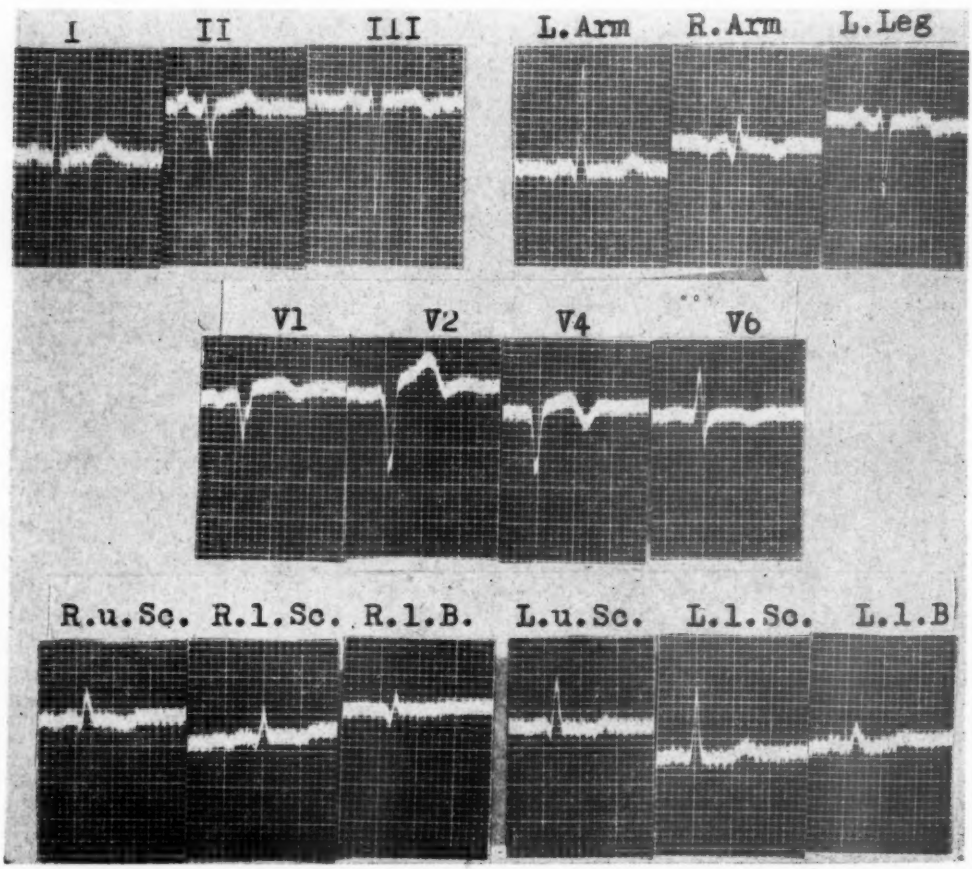


Fig. 9.—A case of anterior infarction with the heart in a horizontal position. L. Z., a man, 69 years of age. For explanation of leads see captions of Figs. 3, 4, and 5.

the heart around any of its axes. In the second place, changes in the size of the heart may occur due to abnormal cardiovascular dynamics such as a decrease in cardiac output, cardiac decompensation, localized dilatation, and other factors. Therefore, although the heart be more or less vertical or horizontal, the typical patterns of right or left axis deviation need not be always observed. The following cases illustrate the validity of these conclusions.

THE Q WAVE IN CASES OF ANTERIOR INFARCTION WITH THE HEART LYING HORIZONTALLY

Fig. 8 is typical of records obtained after anterior infarction when the heart lies horizontally. The characteristic patterns of infarction are observed in the left arm lead and Lead I, whereas the left leg lead and Leads II and III are typical of the patterns found with a horizontal heart. The biphasic right arm potential is suggestive of the fact that the apex of the heart has been displaced backward. This would further serve to make the left leg lead face the right ventricle. Fig. 9 is the record of another case in which infarction occurred and the heart lay horizontally. This is the record of a 69-year-old man, taken several months after his attack. Standard and unipolar extremity leads are what one would expect to find in a normal horizontal heart. There are no signs of infarction in these leads, because the small Q wave is a normal phenomenon with a horizontal heart. However, the precordial leads are typical of anterior infarction.

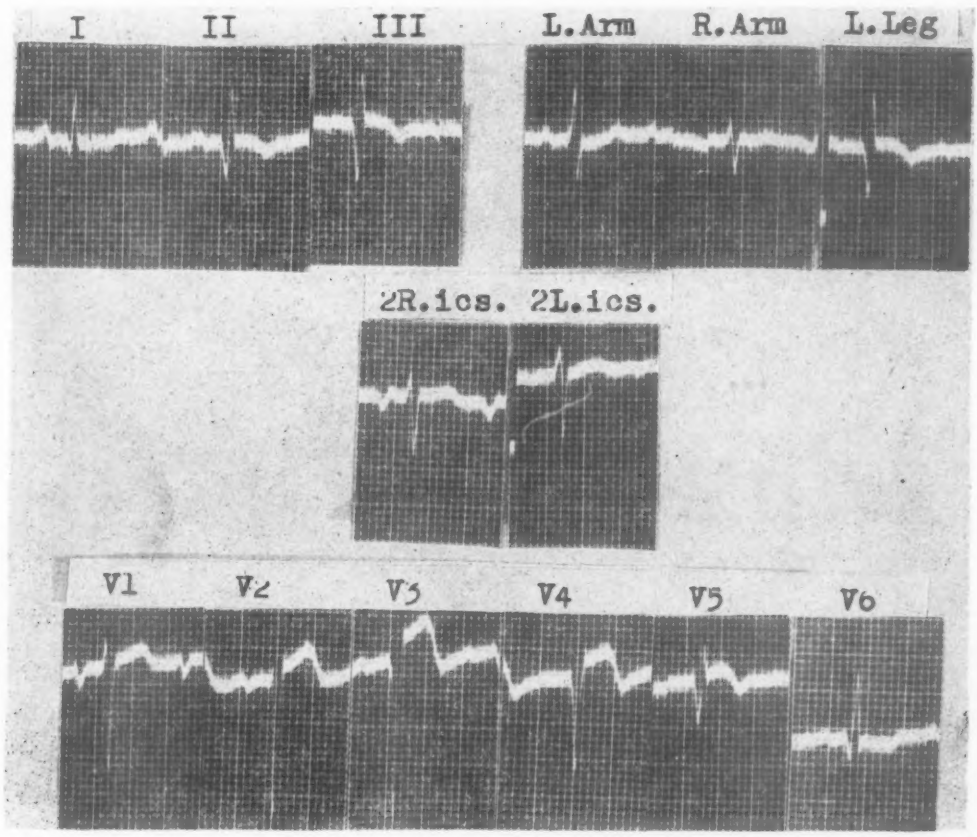


Fig. 10.—Case of anterior infarction with the heart in a vertical position. Y. G., a woman, aged 61 years. For explanation of leads see captions of Figs. 3, 4, and 5.

THE Q WAVE IN CASES OF ANTERIOR INFARCTION WITH THE HEART LYING VERTICALLY

Fig. 10 is the record of a 61-year-old woman who had an acute myocardial infarction several months before the record illustrated was taken. Precordial and chest leads indicate that the patient was suffering from an anterior infarction, although the standard and unipolar extremity leads are typical of posterior infarction. In spite of the fact that a small Q_1 wave is present, the left arm lead begins with an upstroke. It might be argued in this case that the anterior infarct had also extended to the diaphragmatic surface of the left ventricle to produce the patterns in Leads II and III; nevertheless the fact remains that the patterns of anterior infarction were not projected to the left arm lead because of the vertical position of the heart. Although this combination of extremity lead

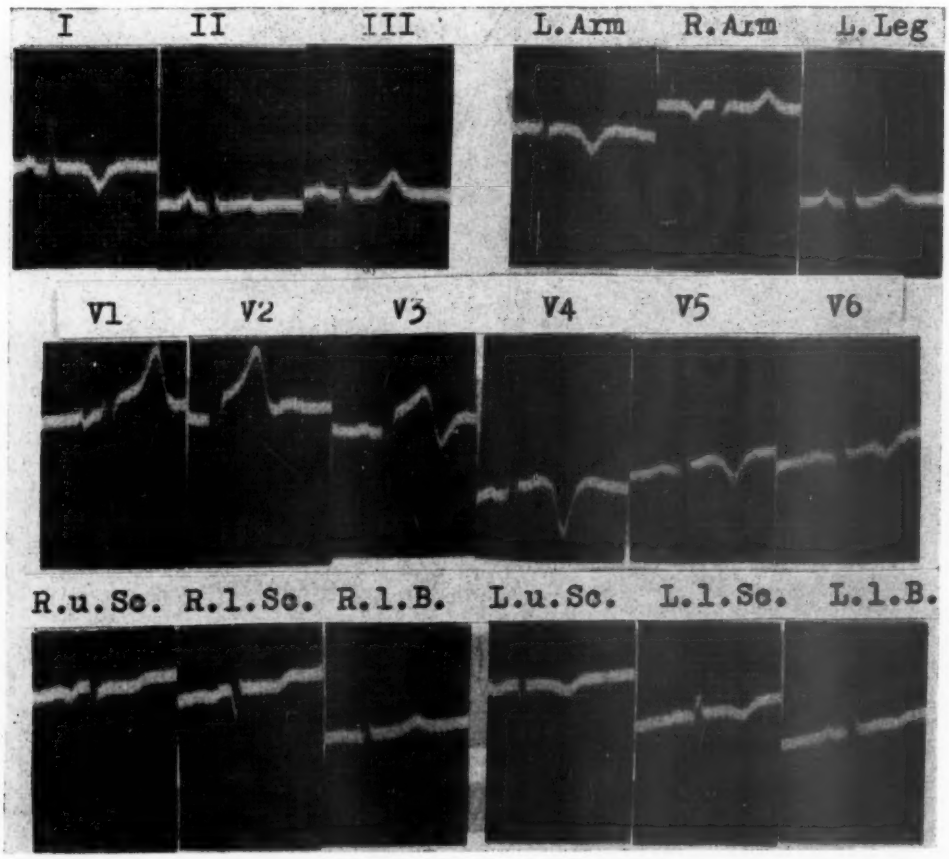


Fig. 11.—A case of anterior infarction with the heart in a vertical position. A. S., a man, 61 years of age. For explanation of leads see captions of Figs. 3, 4, and 5.

and precordial lead patterns is not common, there were five such cases in the series. Fig. 11 is the record of another case of anterior infarction when the heart lay vertically. This was a 61-year-old man who had an acute attack a week prior to the time the record was taken. Standard leads show a typical coved T_1 wave without a Q_1 deflection; whereas in Leads II and III, the typical pattern found in a vertical heart is present: namely, a small Q wave, a high R wave, and an upright T deflection. Study of the precordial leads shows the elevation of the RS-T complex in Leads V_3 and V_4, without Q waves. In the precordial Leads V_5 and V_6, small Q waves appear with the elevated RS-T complex. These Q waves, however, are no deeper than the Q waves of

the left leg lead and the unipolar leads from the lower back. Careful exploration of the surface of the body in this patient disclosed no region which had deep Q waves in association with an elevated RS-T complex. The deep Q wave in the unipolar lead from the angle of the right scapula (*R.l.Sc.*) is what one ordinarily finds in a vertical heart.

THE Q WAVE IN CASES OF POSTERIOR INFARCTION WITH THE HEART LYING VERTICALLY

In a normal or hypertrophied vertical heart, the left ventricle ordinarily faces the left leg lead, and Q waves occur in this lead and in Leads II and III. Furthermore, the T waves in such cases may also point downward in the absence of myocardial infarction. However, elevation of the RS-T segment will not be noted unless infarction has occurred. Fig. 12 illustrates a case of posterior infarction when the heart was more or less vertical. This is the record of a 59-year-old man taken four days after myocardial infarction. Although the left leg lead and Leads II and III have high R waves, there is a high R wave also in the left arm lead and in Lead I, a fact not ordinarily encountered in a vertical heart. Marked elevation of the RS-T segment in the left leg lead and Leads II and III, and marked depression of the RS-T segment of the left arm lead, Lead I, and of the RS-T segments of precordial Leads V_3 and V_4 occur. Precordial Leads V_5 and V_6 have small Q waves, high R deflections, and upright T waves, indicating that the electrodes at these points are facing the left side of the septum and a portion of the normal epicardial surface of the left ventricle.

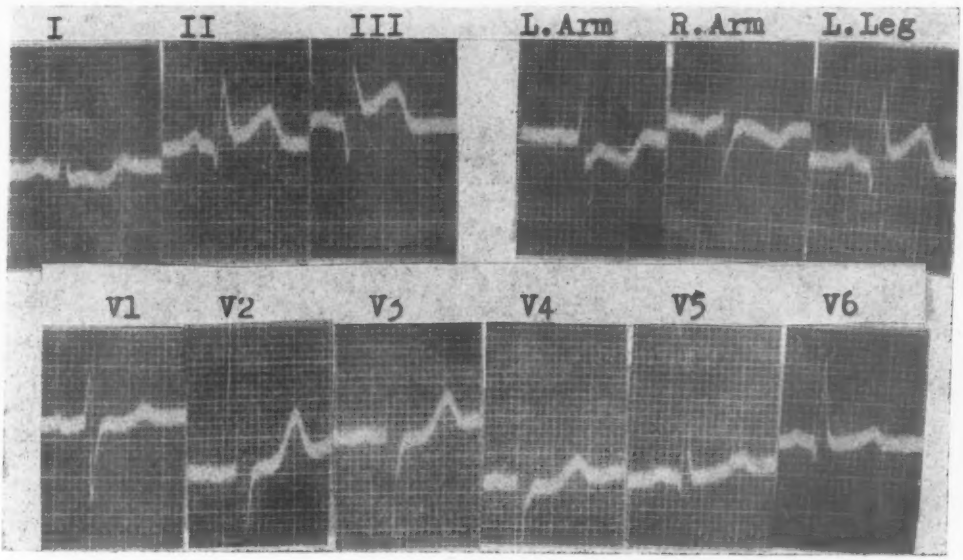


Fig. 12.—A case of posterior infarction with the heart in a vertical position. J. W., a man, aged 59 years.

THE Q WAVE IN CASES OF POSTERIOR INFARCTION WITH THE HEART LYING HORIZONTALLY

Fig. 13 illustrates a case where the peculiarities in the position of the heart produced an unusual distribution of potentials. This is the record of a 62-year-old white man who had been admitted to the hospital for an attack of infarction two days prior to the time the record was taken. The standard and

unipolar extremity leads suggest anterior infarction with the heart in a horizontal position (a Q wave in the left arm lead and an RS deflection in the left leg lead).

Precordial leads are unusual in that the depression of the RS-T segment in leads V_2, V_3, and V_4 indicates that the site of the infarct was certainly not on the anterior or medial surface of the left ventricle. The normal configuration of precordial Lead V_6 also indicates that the left lateral wall of the left ventricle was normal, so one must assume that the infarct lay on the posterior wall of the left ventricle but was transmitted to the left arm lead, because of the horizontal position of the heart. Such a record is most unusual. A more usual type of pattern in posterior infarction with a horizontal heart is seen in Fig. 14. This is the record of a 58-year-old man who had suffered an acute

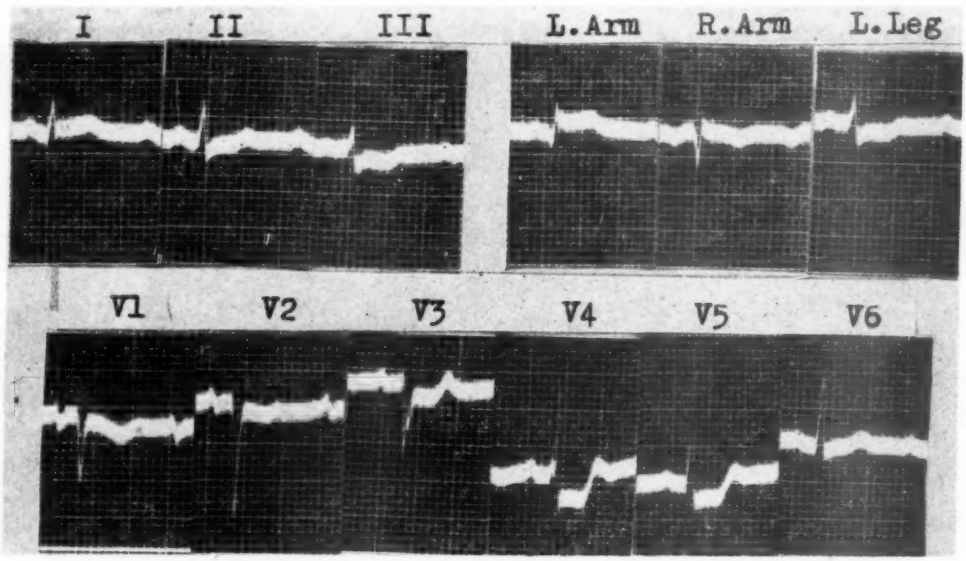


Fig. 13.—A case of posterior infarction with the heart in a horizontal position. B. V. D., a man, aged 62 years.

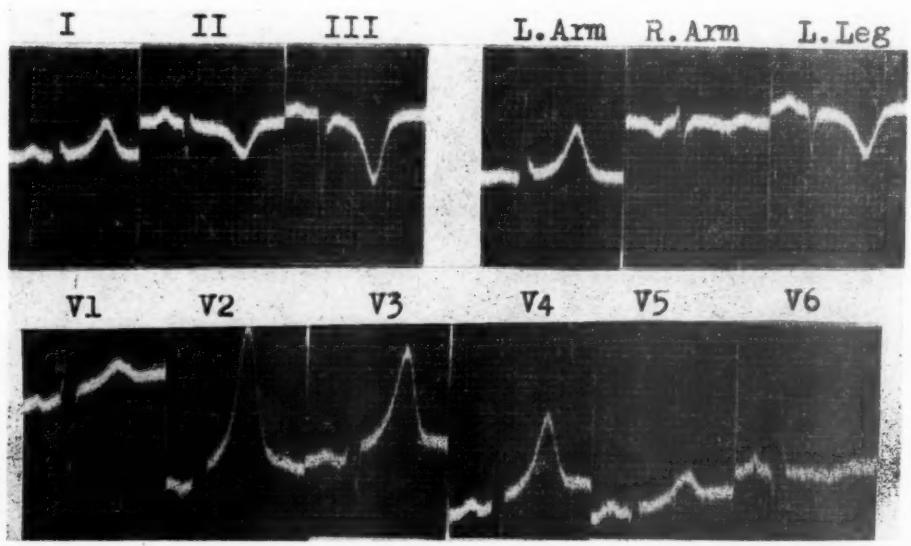


Fig. 14.—A case of posterior infarction with the heart in a horizontal position. L. K., a man, aged 58 years.

attack of infarction about three weeks before this record was taken. The high R wave with a very small Q wave in the left arm lead indicates that the heart is lying horizontally, as does the similarity between the pattern in the left arm lead and precordial Lead V_5. The left leg lead and Leads II and III show a deep Q deflection with coved T waves. If the position of the heart were typically horizontal, the left leg lead would face the right ventricle and therefore no Q waves would be present. The Q wave in the left leg lead can therefore be explained by the fact that the apex of the heart has been pushed forward, allowing the left leg lead to face the left ventricle. Further evidence for this is the pattern in the right arm lead, which is similar to leads from the right upper chest, and the similarity between the abdominal wall potentials (not shown) and the left leg lead.

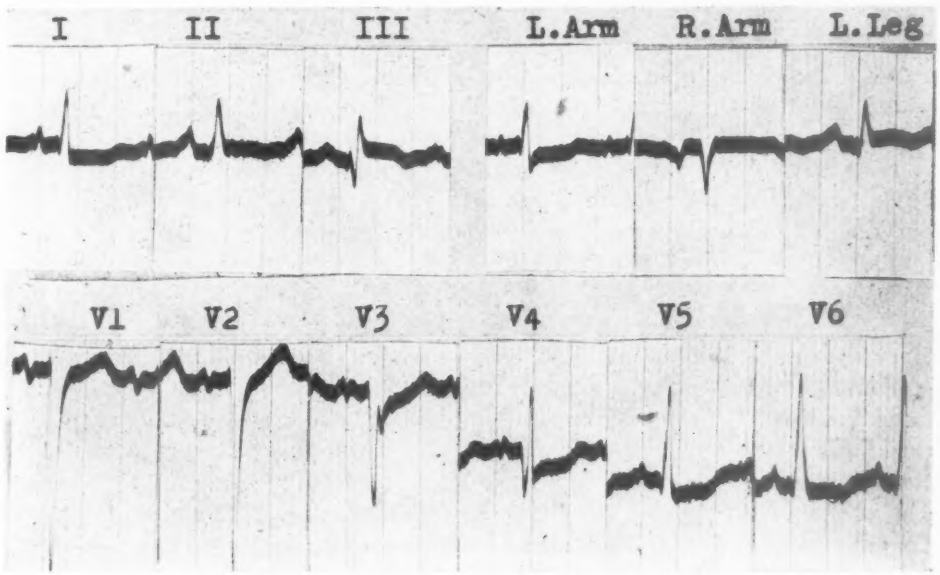


Fig. 15.—A case of multiple infarctions. E. M., a man, aged 49 years.

THE Q WAVE IN CASES OF COMBINED ANTERIOR AND POSTERIOR WALL INFARCTION

Fig. 15 is the record of a 49-year-old man who entered the hospital because of an acute attack of myocardial infarction two days before the record was taken. There was a history of a previous attack several years earlier. The elevation of RS-T segment in the left leg leads and Leads II and III, and its depression in the left arm lead and Lead I, suggest the presence of an acute posterior infarction. Q waves are also present in the left leg lead and Leads II and III, but they are small. The absence of the Q wave in the left arm lead is also usual in posterior infarction. Study of the precordial leads show the marked RS-T depressions in Leads V_2, V_3, V_4, V_5, and V_6 which are typical of an acute posterior infarction, but the deep Q deflection in Lead V_4 suggests the presence of an old anterior infarct. The Q wave of Lead V_4 was not transmitted to the left arm lead, however, because of the position of the heart.

THE Q WAVE IN CASES OF BUNDLE BRANCH BLOCK

Right Bundle Branch Block.—In right bundle branch block the left side of the septum is the first portion of the ventricle to be activated. Therefore unipolar leads facing the left ventricle will record a Q wave. When the heart is

horizontal the left arm lead and Lead I will have a Q wave, and when the heart is vertical the left leg lead and Leads II and III will record a Q wave.[7] Infarction of the left ventricle, complicated by right bundle branch block, does not prevent the Q waves from appearing.[12]

Left Bundle Branch Block.—In left bundle branch block, the right side of the septum is activated first. A unipolar lead overlying, or facing, the left ventricle, therefore, will record an initial upward deflection.[7] When the heart is horizontal, the left arm faces the left ventricle and the left arm lead and Lead I begin with an upstroke. When the heart is vertical the left leg lead and Leads II and III begin with an upstroke, and the left arm lead and Lead I may be entirely downward.[7, 12] Such a pattern is, however, quite rare. Infarction of the left ventricle complicated by left bundle branch block is characterized by the disappearance of the Q waves, even from unipolar leads overlying the infarct. The cause of this is that the left side of the septum is positive at the onset of the QRS deflection. It has been stated that in such cases, if the septum is also infarcted, a Q wave may be seen even with the left bundle branch block.[12] I have had no experience with cases of this type. In a recent paper, cases of left bundle branch block with a Q_1 were discussed.[17] Although no records were presented, I reviewed the cases in the literature cited in this paper. I do not think that such records represent left bundle branch block. Further discussion of this problem is presented elsewhere.[7]

DISCUSSION

The presence or absence of Q waves would be a matter of academic importance were it not for the fact that Q waves are an important sign of myocardial infarction and that, after the infarct has healed, they may constitute the only sign that infarction had occurred. Statistical surveys of the incidence of the various Q-wave combinations have not been too successful in providing a means of differentiating a normal from an abnormal Q wave in the standard leads. One of the reasons for this is the fact that the Q deflection in the standard leads may be the result of a variety of combinations of potential. Another reason for this is that the Q deflection is essentially a normal wave. Basically the Q wave can only be considered abnormal if it constitutes the main ventricular deflection in a unipolar lead overlying the epicardial surface of the left ventricle. In a case of anterior infarction the left arm lead usually faces the infarct and consequently a deep Q wave and coved T deflection will appear in the left arm lead and Lead I. However, it is known that, in a horizontal heart, a Q wave may occur (with a high R deflection and with a downward T wave); and, when the heart is vertical, the left arm lead may consist of a QS deflection and a downward T wave (Fig. 16).

We therefore attempted to determine statistically if the Q wave in the left arm Lead due to infarction might have different characteristics than the Q deflection of the vertical or horizontal heart. The Q-LA deflection was studied in fifty cases of anterior infarction and in one hundred cases where the heart was either normal or hypertrophied. In these cases the duration of the Q wave was measured in the manner previously described. The proportion between the depth of the Q wave to the amplitude of the entire QRS complex was also determined. The depth of the Q or S wave was measured from the lower edge of the string shadow at the end of the P-R interval to the apex of the Q wave. The height of the R deflection was measured from the upper edge of the string shadow at the end of the P-R interval to the apex of the R wave. The values of R and Q (or S, if an S wave occurred and was deeper than the

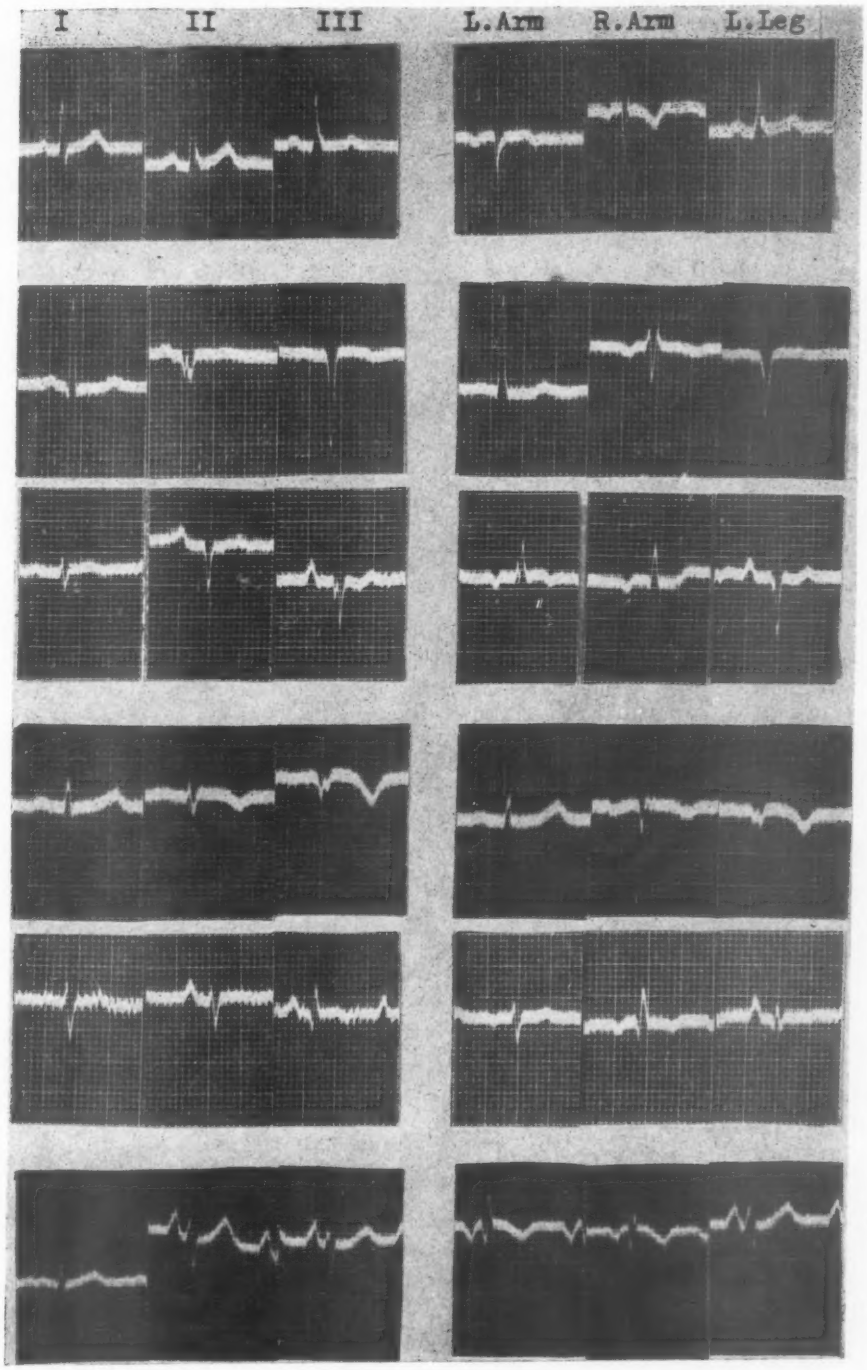


Fig. 16.

a.

Fig. 17.

b.

a.

Fig. 18.

b.

Fig. 19.

Fig. 16.—A normal vertical heart. M. B., a man aged 29 years. Note the QS deflection in the left arm lead.

Fig. 17.—Two cases showing QS deflections in the left leg lead. *a*, A case of old posterior infarction. I. G., a man, aged 85 years. *b*, A case of bilateral pulmonary tuberculosis. A. B., a man, aged 27 years.

Fig. 18.—Two cases showing a W-shaped QRS complex in the left leg lead. *a*, A case of posterior infarction. A. D., a man, aged 53 years. *b*, A case of chronic asthma and emphysema. J. M., a man, aged 57 years.

Fig. 19.—A case showing a Q wave and downward T deflection in the left arm lead in the absence of infarction. S. K., a man, aged 61 years. Chronic asthma and emphysema. The QR deflection in the right arm lead indicates that the apex of the heart has been displaced backward. Note the similarity of the left arm and right arm leads, and the negative P deflection of the left arm lead.

Q wave) were then added to get the amplitude of the QRS complex. The relation of the depth of the Q wave to the amplitude of the QRS complex was expressed as a percentage.

The characteristics of the T wave and RS-T segment were noted. In fifty cases of anterior infarction, eighteen had a Q wave with a duration of 0.04 second or more, and an amplitude of 30 per cent or more of the entire QRS complex. Five cases had a QS deflection. However, in twenty-seven cases, Q-LA had a duration of less than 0.04 second and an amplitude of less than 30 per cent of the QRS complex. Five of the series of one hundred normal cases had a Q wave with a duration of 0.04 second. In the remaining, the duration of the Q-LA interval was less than 0.04 second. In seven cases, a QS wave was noted in the absence of myocardial infarction (Figs. 6 and 16).

We can therefore conclude that a wide, deep Q wave in the left arm lead, with a depth of 0.04 second or more, comprising 30 per cent or more of the entire QRS complex (excluding a QS deflection), in association with a coved T wave is a presumptive sign of infarction, although this pattern may be present in the absence of infarction, and infarction may be present in the absence of this pattern. In such cases without infarction, the P wave is likely to be very negative in the left arm lead (Fig. 19). Inasmuch as a diagnosis of anterior infarction can be made more advantageously with unipolar precordial leads, the use of the characteristics of the Q wave in the left arm lead as a sign of infarction is not to be recommended. However, in the case of posterior infarction of the left ventricle, the infarct usually overlies the diaphragm, and it therefore is difficult to obtain unipolar leads overlying the infarct, unless esophageal leads are used. The left leg lead, however, ordinarily faces the infarct, and has the characteristic deep Q wave and elevated RS-T segment in cases of posterior infarction. A Q wave in the left leg lead is, as we have pointed out, very often a normal phenomenon. For this reason, we analyzed fifty cases of posterior infarction and one hundred cases of normal and hypertrophied hearts with a Q wave in the left leg lead in a manner similar to that used in cases of anterior infarction. The results were significant. We found thirty of the fifty cases of posterior infarction with a Q wave whose amplitude equaled or exceeded 40 per cent of the entire QRS complex. In these cases, the T wave was coved in all but three. These latter were instances of old healed posterior infarction. In all but one of the thirty cases, the duration of Q was 0.04 second or more. Six cases had a QS deflection, with a wide Q wave. Three of these cases had an upward T wave (Fig. 17,*a*). Nine cases had a small W-shaped QRS deflection with a coved T (Fig. 18,*a*). In most of these it was difficult to measure the width of the Q wave. Five cases had a small Q wave whose amplitude was less than 40 per cent of the entire QRS complex. In one case, the width of the Q wave was also less than 0.04 second. All five cases, however, had elevation of the RS-T segment and coving of the T wave. Of the one hundred normal records, only two had a Q wave which was 40 per cent or more of the entire QRS deflection. The width of the Q wave in these two cases was less than 0.04 second. Furthermore, the width of the Q wave in all but three of the one hundred cases was within 0.04 second. There were four cases with a QS deflection (Fig. 17,*b*) and five cases with a small W-shaped QRS complex (Fig. 18,*b*).

It is therefore concluded that, when the Q wave in the left leg lead has a duration of 0.04 second or more, and has an amplitude of 40 per cent or more of the entire QRS complex (and is not W-shaped or does not consist of a QS deflection), such a record indicates posterior infarction. In most of these cases the

RS-T segment will be elevated or the T wave will be coved, but, after healing of the infarct has taken place, the T deflection may become upright.

CONCLUSIONS

In cases of normal conduction or right bundle branch block, the Q wave, as recorded in unipolar leads, is due to the fact that the left side of the interventricular septum is activated before the right side.

The characteristics and depth of the Q deflection varies with the position of the electrode. If the electrode tends to face the left ventricular cavity, the entire QRS complex may consist of a QS deflection. The duration of the Q wave, therefore, will be 0.04 second or more. If the electrode faces the epicardial surface of the left ventricle, the Q deflection is small in comparison with the tall R wave which follows (less than 30 per cent of the entire QRS complex) and its width is less than 0.04 second.

There are other mechanisms by which a Q wave may appear. If a lead which faces the right ventricle and ordinarily records an RS deflection is placed so that it tends to lie on the same plane as the interventricular septum, the initial activity in the septum, running at right angles to the plane of the septum, will be without effect on the electrode, and the initial upward deflection may not be recorded, so that the QRS appears as a QS deflection.

In infarction of the left ventricle involving the greater thickness of a portion of the wall, an electrode overlying, or facing, the infarct will record not only the initial negativity of the left side of the septum but, because the infarcted muscle has lost its electrical activity, the infarct acts like a window in the ventricular wall and the remaining portion of the QRS complex is negative, which is the potential of the ventricular cavity during the inscription of the QRS complex.

Since Q is an initial downward deflection, its presence in unipolar extremity leads has a different meaning than a Q wave in the standard leads. However, certain relations between standard and unipolar leads exist in that Leads II and III tend to resemble the left leg lead, and Lead I tends to resemble the left arm lead.

Variations in the location of the Q deflection in the extremity leads depends on the position of the heart. If the heart lies horizontally, the left arm lead faces the epicardial surface of the left ventricle and a Q wave with a tall R deflection will usually be seen in the left arm lead and Lead I. If the heart lies vertically, the left leg lead usually faces the epicardial surface of the left ventricle and a Q wave and high R deflection appear in the left leg lead and Leads II and III. However, if the apex of such a heart is displaced backward, the left leg lead faces the right ventricle and the Q waves disappear. If a vertical heart has marked clockwise rotation around its long axis, small Q waves may appear in precordial leads to the right of the sternum.

With infarction of the ventricles, Q waves will not appear if the infarct involves the right ventricle or an area near the plane of the interventricular septum.

With infarction of the anteriorlateral surface of the left ventricle the RS-T segment elevation may be observed with small Q waves which are due (as in a normal heart) to the activation of the left side of the septum, or with very deep QS deflections which are due to the fact that the greater thickness of a portion of the muscle wall has been infarcted.

If the entire surface of the left ventricle is not infarcted, regions will be found overlying normal muscle in which a small normal Q wave may be

recorded with a high R deflection and upright or high T wave (or with a depression of the RS-T segment).

Although the patterns of anterior infarction are usually transmitted to the left arm lead and Lead I, and the patterns of posterior infarction are usually transmitted to the left leg lead and Leads II and III, variations in the distribution of the patterns may occur because of the position of the heart. Thus, with anterior infarction, if the heart be vertical, Leads II and III may record the characteristic Q wave and elevated RS-T segment. Similarly, with posterior infarction, if the heart be horizontal, Lead I may record the Q wave and elevated RS-T segment.

The distribution of the Q wave in cases of right bundle branch block is similar to that in the normal heart. Right bundle branch block, complicating infarction of the left ventricle, does not result in the disappearance of the characteristic Q waves.

In cases of left bundle branch block, the initial deflection in leads facing the left ventricle is upward; consequently, left bundle branch block complicating infarction of the left ventricle results in the disappearance of Q waves.

In left bundle branch block without infarction, the heart usually lies horizontally, and the left arm lead and Lead I do not record a Q wave, although a Q deflection may be present in the left leg lead and Lead III.

Statistical study of the Q waves of the unipolar extremity leads in normal cases and after infarction allows certain conclusions to be drawn: In the left arm lead, if the Q deflection comprises more than 30 per cent of the entire QRS complex, has a width of 0.04 second or more, and is associated with a downward T wave, such a pattern is usually due to anterior infarction, although such a pattern may occasionally be seen in a vertical heart with marked clockwise rotation and displacement of the apex of the heart backward (Fig. 19). If the pattern is due to a vertical heart, the P wave is usually deeply negative, a finding which does not ordinarily occur with infarction. Furthermore, study of the precordial leads in such cases will establish the presence or absence of an infarct.

In the left leg lead, if the Q deflection has an amplitude of 40 per cent or more of the entire QRS complex, and it has a duration of 0.04 second or more and is associated with a downward T deflection, such a pattern is usually due to posterior infarction. However, similar records, especially if the QRS complex consists of a QS deflection or of a small W-shaped complex, are occasionally met with in cases without infarction. Such records ordinarily have very large P waves and the precordial leads in such cases give evidence usually of enlargement of the right ventricle.

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ADDENDUM

Myers and Oren, in a recent paper ("The Use of the Augmented Left Leg Lead in the Differentiation of the Normal From the Abnormal Q Wave in Standard Lead III," Am. Heart J. 29: 708, 1945), studied the relation between the Q wave in the left leg lead and the R wave in the left leg lead in cases of myocardial infarction, instead of determining the relation between the Q wave and the entire QRS complex, as we did. They found that, when Q_{LL} had 25 per cent or more the amplitude of R_{LL}, a diagnosis of posterior infarction could be suspected from this alone.

We reinvestigated our measurements in the left leg lead in cases of posterior infarction, using the relation between Q and R instead of between Q and QRS. We found that, when Q_{LL} had 60 per cent or more the amplitude of R_{LL} and was 0.04 second or more wide, myocardial infarction was usually present unless the left leg lead showed a QS pattern or a W-shaped QRS complex.

DETERMINATION OF CIRCULATION TIME; UNSUITABILITY OF PAPAVERINE

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NUMEROUS methods are available for determining the velocity of blood flow. Subjective methods for estimating the circulation time have the important disadvantage that the cooperation of the patient is required. Objective methods on the other hand require, in some instances, rather special apparatus. With both methods the substance introduced into the blood stream may prove toxic.

Sodium dehydrocholate (Decholin) has been used for measuring the circulation time. In view of the fact that this method depends on a subjective re-

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sponse, the patient's signalling the development of a bitter taste in the mouth, and because occasional unpleasant reactions have occurred (Leys[1]), we have sought an easy objective method.

Papaverine hydrochloride was used by Elek and Solarz,[2] who reported successful determination of circulation time by injecting this drug into an antecubital vein and noting the end point, described as a sudden deep inspiration, with a sigh or exclamation, commonly followed by flushing of the face, mild dizziness, and tachypnea. No other reports on this method appear in the literature.

We have used the method described by the authors,[2] with one exception: the dose of papaverine hydrochloride, 40 mg., was administered in solution in 1.6 instead of 1.25 cubic centimeters. The method was unsatisfactory in our hands. The results are described.

RESULTS

Fifty patients, hospitalized for various disorders and aged 20 to 80 years, were used in this study. In thirteen patients (26 per cent) the end point was good—a deep inspiration occurred. In seventeen (34 per cent) the reaction was not satisfactory—the end point was very difficult to determine. In twenty (40 per cent) no reading at all could be obtained.

Duplicate readings were made in those cases in which a sharp end point was observed. The results of the tests with satisfactory end points are given in Table I.

TABLE I. DETERMINATION OF CIRCULATION TIME WITH PAPAVERINE

DIAGNOSIS	FIRST READING (SEC.)	SECOND READING (SEC.)
Thyrotoxicosis	19	18½
Hemophilia	19	18
Hemolytic anemia	15	20
Pernicious anemia	23	21
Pneumonia	17½	18
Bronchiectasis	18½	23½
Pleural effusion	20	20
Peripheral neuritis	16	21
Peripheral neuritis	20	21½
Hypertensive heart failure	18½	17
Mitral stenosis with congestive failure	19	15
Dysentery	24	24½
Abdominal tumor	23	21

COMMENT

The injection of papaverine hydrochloride to estimate the circulation time has not proved successful in our hands. The following difficulties were encountered.

1. In a major proportion of patients no satisfactory end point was obtained.

2. In patients in whom sharp end points were obtained, duplicate determinations differed by as much as 5 seconds.

3. No satisfactory differences in circulation time occurred in patients with thyrotoxicosis, congestive heart failure, or anemia or in normal subjects which were of any clinical value.

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ELECTROCARDIOGRAPHIC FEATURES OF MYOCARDIAL INFARCTION AS AFFECTED BY INVOLVEMENT OF THE SEPTUM AND BY COMPLETE AND INCOMPLETE TRANSMURAL INVOLVEMENT

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IT HAS seemed to the authors that many of the current theories as to the causation of abnormalities of the S-T junction and T wave and the appearance of the Q and the Q-S deflections after myocardial infarction are in need of testing against the findings in human autopsy material. It was decided, therefore, to review a series of cases, correlating the exact situation and extent of the infarcted areas with the electrocardiographic findings. Leads I, II, III, and IVF were recorded in this series.

The usual pathologic descriptions, as found in autopsy reports, were insufficiently detailed for this purpose and so it was thought advisable to confine the study to a group of hearts that could be re-examined because they had been preserved in the Pathological Department of The New York Hospital. It was possible to obtain eleven hearts of patients who had died of a recent infarction and one with an old healed infarct. All but one of these patients had died after a severe, acute attack due to coronary thrombosis which occurred within three to fifteen days after the initial symptoms developed. The one with a healed infarct died of metastatic carcinoma two years after an attack of coronary thrombosis. These hearts were examined with the assistance and usually with the actual personal cooperation of Dr. William Dock. When he was not available, other members of the Pathological Department were consulted. The exact location of the infarct in relation to posterior, lateral, and anterior walls and septum was noted and it was observed whether or not the epicardial or endocardial muscle layers were affected throughout the area of the infarct. The pathologic findings in these cases are summarized in Table I.

TABLE I. DISTRIBUTION OF NECROSIS AND SCARRING

	CASE											
PORTION OF HEART	1	2	3	4	5	6	7	8	9	10	11	12
Subepicardial	+	.	.	.	.	sc	.	.	.	.	.	.
Anterior wall	+ sc	+	+	+	.	.	.	.	.	.	.	.
Subendocardial	+	+	.	+	+	.	.	.	.	.	.	.
Anterior septum	+ sc	+	.	+	+	sc	.	.	sc	.	sc	.
Subepicardial	.	.	.	.	.	.	.	+	.	+	+	sl
Posterior wall	.	+	sc	.	.	.	sc	+	+ sc	+	+	+
Subendocardial	.	.	.	.	.	.	.	+	+	+	+	sl
Posterior septum	.	.	.	.	.	.	.	.	.	+	+	.
Lateral wall	.	.	.	sl	.	+	sc	.	.	.	.	.

+ indicates necrosis.
sc indicates scarring.
sl indicates a small area of necrosis only.

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CLINICAL AND ANATOMIC FINDINGS

CASE 1.—On the morning of the day of admission, the patient had a severe coughing spell, collapsed, and became unconscious. On admission, the heart sounds were faint, almost inaudible. The patient died on the day after admission after gradually increasing respiratory difficulty and weakening pulse. The heart was not enlarged. The right coronary artery was thrombosed, and the anterior descending branch was also thrombosed; the circumflex branch was patent. There was extensive old scarring in the anterior part of septum and the adjacent anterior wall and apex. A new infarct was noted in the median portion of the anterior wall adjacent to the old scar, affecting the entire thickness of the muscle.

CASE 2.—The patient had had heart disease for five years. Four years previously, he was said to have had myocardial infarction. He was known to have had blood pressure measurement of 220/130, fifteen months before the present illness. The patient was admitted in heart failure of one month's duration, with auricular fibrillation with an apical rate of 126 per minute. On the third hospital day, he developed severe precordial pain radiating into both arms. The blood pressure measurements became difficult to obtain; the pulse was almost imperceptible; and the respirations were 48 per minute. The patient died five days later after progressively increasing pulmonary congestion. The heart was much enlarged. The right coronary artery was patent; the anterior descending branch was thrombosed; the circumflex branch appeared patent; and a small branch in the lateral wall was thrombosed. There was a large, recent infarct of the anterior wall and septum, reaching the endocardium in both areas, extending to posterolateral wall through the apex. The pericardium and endocardium in the posterior wall, and the epicardium were not involved.

CASE 3.—Three days before admission, the patient experienced severe pain in the chest radiating to the right shoulder and arm; nausea and vomiting. He was very short of breath. The cough and shortness of breath grew worse. He entered the hospital on the third day, at which time he was cyanotic and orthopneic. The heart sounds were faint, and the lungs showed numerous moist râles; the ankles showed 1 plus edema. He continued about the same for five days and then died suddenly. The heart was slightly enlarged. The right coronary artery appeared to be narrowed at the orifice by syphilitic aortitis; otherwise it was patent. The anterior descending branch was narrowed and a large subsidiary branch of this was also narrowed. The circumflex branch was thrombosed; a branch of the circumflex artery appeared narrowed. There were old scars in the posterior wall. A large infarct was found in the anterior wall, extending to the lateral wall but neither the endocardial nor the pericardial surfaces were involved. The infarct did not extend into the septum.

CASE 4.—The day before admission, the patient experienced a severe attack of epigastric pain, radiating laterally around the lower ribs and to the arms. By evening these pains were almost continuous. He was awakened at 1:00 A.M., on the day of admission, by an especially severe and prolonged pain. On the sixth day, the temperature was 39.6° C., the pulse was 90 per minute, the respirations were 20, and the blood pressure measured 130/85. On the second day after admission, he developed persistent, aching, precordial pain and a pericardial rub was heard. This continued for only two or three days, but the pain subsided more slowly. He seemed to be progressing in a satisfactory manner when suddenly, on the twentieth day after the infarct, he developed an attack of severe dyspnea, with a markedly irregular pulse, which became very fast. Shortly thereafter he died. The heart was not enlarged. The right coronary artery was patent. The anterior descending branch was thrombosed; the circumflex branch was open. There was a recent infarct in the anterior portion of the septum on the endocardial surface only, extending into the anterior wall of the left ventricle as far as the lateral wall. The process was entirely subendocardial. The epicardium was involved only laterally and, there, not extensively.

CASE 5.—Two days before admission, the patient had intermittent attacks of precordial pain which recurred on the day preceding admission. He entered the hospital with a temperature of 38.4° C.; pulse rate 100 per minute, and respirations 20. The blood pressure measured 165/100. The leucocytes were 32,000 per cubic millimeter. There were minimal râles in the bases of the lungs. His course was very satisfactory for nine days, when he suddenly became pale and very short of breath; he died in a short time. The heart was small. The right coronary artery and circumflex branch of the left were patent. The left descending branch was open but the septal branch was thrombosed. An infarct of the anterior portion of the septum was observed extending to the apex, but not reaching the epicardial surface. It was subendocardial in the left ventricle and also to a lesser extent in the right ventricle. No involvement of the anterior wall of the left ventricle or of the posterior portion of the septum was noted.

CASE 6.—The day before admission, the patient had severe pain beneath the sternum and over the precordium, lasting until the time of admission. The temperature ranged between 37.8° C. and 39° C.; the pulse rate was 92 per minute; and the blood pressure measured 132/88 (the systolic value had been 260 four years previously). The white blood cells were 17,000 per cubic millimeter. The course was uneventful for eight days but, on the ninth day after admission, there was increasing respiratory distress. The patient died on the following day, eleven days after the attack. The heart was slightly enlarged. The right coronary artery showed a recent thrombus; the anterior descending branch was patent and the circumflex branch was the site of a recent thrombus. Old scars were seen in the anterior portion of the septum, extending to the epicardial surface, but the endocardium was not reached. There was a recent extensive lateral infarct, extending from 2 cm. lateral to the anterior margin of the septum, around to the posterior wall. The posterior part of the septum was not involved. The infarct really lay more posteriorly than anteriorly, definitely posterolateral.

CASE 7.—The patient had experienced an attack of coronary thrombosis two years before admission. The symptoms were severe precordial pain, shortness of breath, orthopnea, weakness, and loss of appetite. Rest in bed had been enjoined for six weeks. The patient was admitted because of disability from carcinoma of the ovary with metastasis. The electrocardiogram was taken on the day after admission, about three months before death. The heart was not enlarged. The coronary artery appeared patent, and the anterior descending branch was narrowed. The circumflex branch was narrowed with one area of closure. The lateral wall, near the apex, was scarred, and the apex was involved in its posterior portion. The septum was not involved.

CASE 8.—The patient was known to have had hypertension for four years before admission. A week preceding admission, gradually increasing weakness and shortness of breath occurred when at rest. Three days before admission, he had slight precordial oppression which lasted several hours. He was admitted with pulse barely perceptible. The temperature was 36.8 ° C. The blood pressure measured 80/60. The heart sounds were weak and the lungs contained numerous moist râles. The temperature was persistently high, and the patient died with increasing shortness of breath and pulmonary congestion on the sixth day after admission. It is noteworthy that this patient did not have a well-defined date of onset.

The heart was not enlarged. The right coronary artery was patent, and the anterior descending branch was open. The circumflex branch was narrowed to 1 mm. in diameter and a superficial descending branch on the posterior aspect was thrombosed. There was an infarct in the posterior wall, involving the epicardial and endocardial surfaces, but the septum was spared. The necrotic area was 3 by 3 centimeters.

CASE 9.—For three nights before admission, the patient had felt precordial pain while in bed. On the night before admission, the pain was unusually severe and was associated with nausea and vomiting. The temperature on admission was 37.4° C., and the pulse rate was 130 per minute. The blood pressure measured 106/74. The maximum temperature during hospitalization was 38.2° C. The patient developed increasing signs of cardiac failure but left the hospital on the seventh day against advice. He died the following night at his home. The heart was much enlarged. One-third of the right coronary artery was occluded. The anterior descending branch was thrombosed. One-half of the circumflex branch was occluded. There was an old infarct of the anterior portion of the septum, with thinning of the apex. There was a fresh infarct involving the endocardium of the posterior wall, but the epicardium and septum were not involved. It would seem that the posterior infarct might have been due to closure of the anterior branch combined with the narrowing of the other blood channels.

CASE 10.—No symptoms referable to the heart had been experienced by this patient who was being treated in the rhino-otolaryngologic clinic by irrigation of the antrum. After returning home from one of these visits, he collapsed and became semicomatose. On admission to the hospital, the heart sounds were almost inaudible, the lungs showed râles at both bases, and the blood pressure was 100/65. The temperature was 38.8° C. The blood pressure gradually fell, and he died on the second day after admission. The heart was somewhat enlarged. There was a thrombus in the right coronary artery; the anterior descending branch showed a recent thrombus. A similar finding was present in the circumflex branch. There were fibrous bands in the anterior portion of the septum. A recent infarct was observed in the posterior wall and the posterior part of the septum, extending to both epicardial and endocardial surfaces.

CASE 11.—The patient was admitted to the hospital with heart failure and hypertension and for eleven days made satisfactory progress under treatment. He then had an attack of severe pain with vomiting, followed by a rise in temperature which went as high as 39.3° C. The blood pressure fell to 110/98. There was an elevated sedimentation rate and a leucocytosis of 19,000 cells per cubic millimeter. The pain subsided and he was making satisfactory progress but died suddenly on the sixth day after the attack. The heart was much enlarged. The right coronary artery showed a recent thrombosis; the left anterior descending branch exhibited an old closure; the circumflex branch was the site of a recent thrombosis. There was old scarring in the anterior wall which did not involve the epicardial layer. A large recent infarct was found in the posterior wall, extending into the septum and into the apex and somewhat laterally, involving both endocardial and epicardial surfaces.

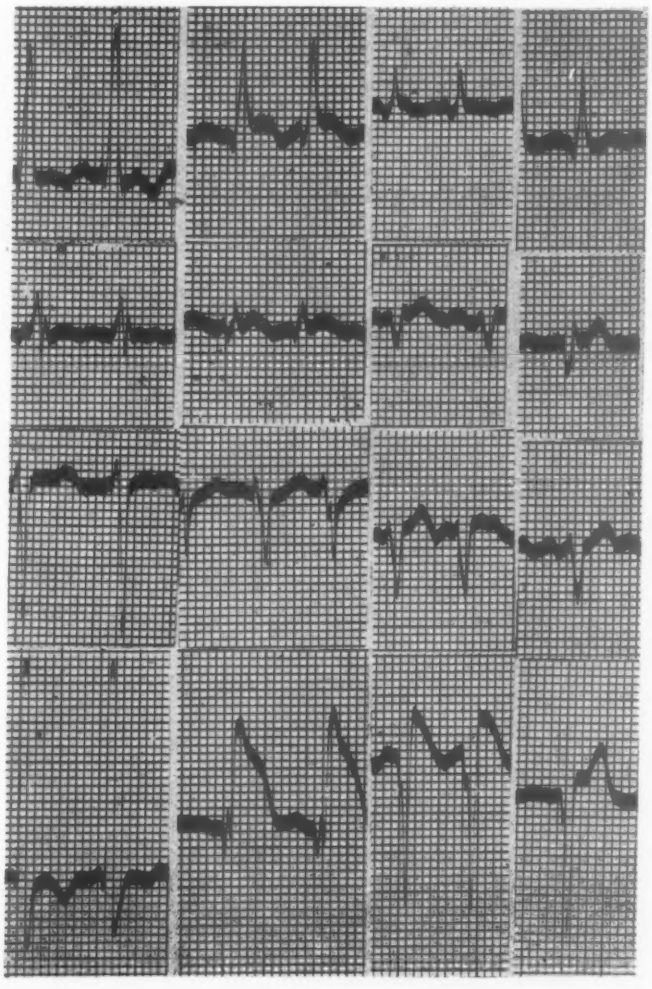
CASE 12.—Two days before admission, the patient experienced an attack of severe excruciating pain in the left side of the chest, extending to the arm. The following day he was able to be up but, on the second day, he had a temperature of 39° C. and felt very weak. He was admitted to the hospital at this time. The blood pressure was 125/75; the pulse rate was 110 per minute; and the respirations were 32. He developed cardiac failure following admission and died on the seventh day. The heart was slightly enlarged. The right coronary artery seemed patent. The anterior descending branch was narrowed; the circumflex branch contained a recent thrombus. There was a large intramural infarct on the posterior wall with lateral extension. Only two small areas, each about 4 by 8 mm., extended to the epicardial surface. The smaller of these reached the endocardium.

ELECTROCARDIOGRAPHIC FINDINGS

Cases 1 and 2 showed areas of infarction involving the anterior wall and the anterior part of the septum. In Case 1 the entire thickness of the anterior wall was necrotic, but in Case 2 the subepicardial fibers were not involved to a depth of 4 millimeters. The electrocardiograms of both these cases showed the typical appearance associated with acute anterior infarction, both in the limb leads and in the precordial lead (Fig. 1,*B*). The Q_1 and $Q\text{-}S_4$ deflections were present in both cases, as well as the usual elevation of the S-T junction in Leads I and IV, with depression in Lead III. It is noteworthy that in Case 2 the subepicardial layers of muscle were not necrotic, because in the records taken after the infarction (Fig. 1,*B*, *C*, and *D*) the precordial lead had lost the R wave (preintrinsic deflection), showing only a large Q-S wave. This feature has been attributed to the effect of a lesion extending entirely through the ventricular wall, yet such a condition was not found in this heart. It is well recognized that the function of muscle is not always indicated by its structural appearance. A damaged portion of heart muscle may give rise to abnormal electrocardiographic features and yet may appear normal on later microscopic examination, provided that the damage has not been too severe or of too long duration. The marked S-T deviation in the early record may indicate a transient phase of damage to these superficial muscle fibers; their ultimate recovery is suggested by the more normal form of T_4 in Fig. 1,*D*. The regression of the early S-T and T-wave changes was unusually rapid in this case, since it almost disappeared from the limb leads in two days (Fig. 1,*C*). One might assume that this rapid regression was associated with a recovery of function in the surviving subepicardial layers, but if this were so, it is surprising that the R wave did not reappear in the precordial lead of the later records (Fig. 1,*C* and *D*) as experimental observations would have led us to expect with such a recovery. It is of interest also that this heart, in addition to the infarct in the anterior wall, had intramural involvement in the posterior wall, not reaching either the endocardial or epicardial surfaces, and that there was nothing in the electrocardiogram to suggest posterior wall involvement.

There were four cases which might be said to represent incomplete anterior infarcts, as the complete thickness of the wall was not involved (Cases

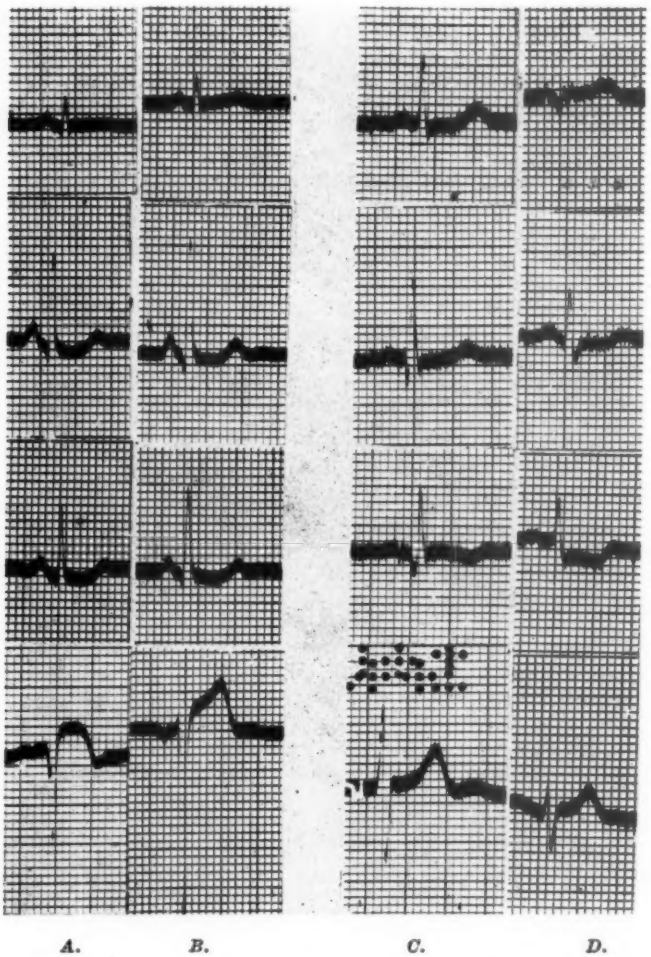
2, 3, 4, and 5). In Case 3, the infarct was entirely intramural, as it involved the deeper layers of the anterior wall, but it did not reach either the endocardial or epicardial surfaces nor did it extend into the septum. A record before infarction (Fig. 2,*C*) showed a normal axis of the QRS complex with Q_2 and Q_3 waves. After infarction (Fig. 2,*D*) the axis of the QRS complex was at the right border of the normal sector, and the Q_3 deflection was absent. The S-T junction in Lead I was +1 mm., and the T wave was upright. The S-T junction in Lead II was –1 mm., and the T wave was inverted. The S-T junction in Lead III was –2 mm., and the T wave was inverted. In Lead IV the QRS, S-T, and T waves showed little change from their previous normal form except in amplitude. The R wave persisted, as might be expected by analogy with experimental results with an anterior infarct not reaching the epicardium, but there was no Q_4 deflection, as would have been expected with such a lesion.[2] It is of interest that the Q_3 deflection was abolished by an intramural lesion of the anterior wall which did not involve the anterior part of the septum. The appearance of the S-T segment and the T waves in the limb leads was much like that seen after anginal attacks,[3] anoxemia,[4] and exercise tests.[5] Considering the four-lead electrocardiogram, one could not definitely say that it indicated an anterior infarction.



A. *B.* *C.* *D.*

Fig. 1 (Case 2).—*A*, Before infarction. *B*, Less than twenty-four hours after the attack. *C*, Two days after the attack. *D*, Five days after the attack. In this and in all subsequent figures, the leads are I, II, III, and IVF, from above downward.

The lesion in Case 4 involved the anterior wall and its endocardial surface, the anterior portion of the septum, and the lateral wall slightly, but not anywhere did it reach the epicardial surface, except in a small area on the lateral wall. The record before infarction (Fig. 3,*A*) showed left axis deviation of the QRS complex with a Q-S_3 wave, an inverted T_1 wave of the coronary type, and a diphasic (±) T_4 wave.



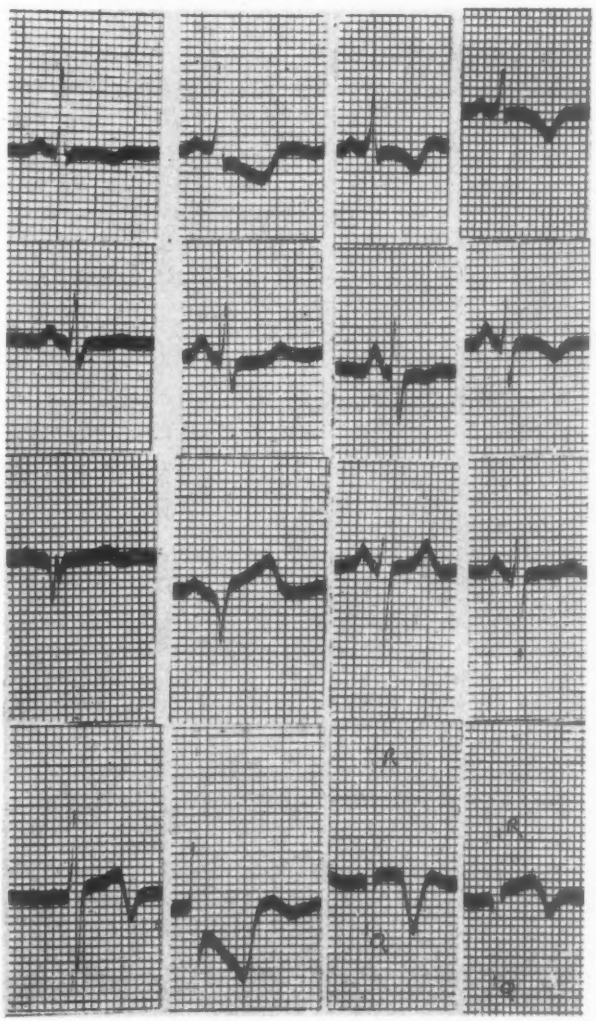
A. *B.* *C.* *D.*

Fig. 2 (Case 5).—*A*, Three days after infarction. *B*, Six days after the attack. *C*, (Case 3). Before the infarction. *D*, Record three days after the attack.

On the day of the infarction, Fig. 3,*B* was obtained. The QRS complex was essentially unchanged; the S-T_1 junction was depressed and the T_1 wave was inverted; the S-T_2 junction was slightly downward, with the T_2 wave positive; the S-T_3 junction was elevated and the T_3 wave was upright; the S-T_4 segment was depressed and the T_4 wave was inverted.

These S-T- and T-wave changes are the opposite of those expected with an anterior wall infarct. It has been suggested on theoretical grounds by Bayley[6] and others that such a reversal of direction may be due to the infarct affecting only the endocardial portion of the anterior wall. The S-T- and T-wave changes closely resemble the appearance found in the acute stage of lateral infarction as described by Wood, Wolferth, and Bellet and also that seen after exercise tests and anoxemia tests.

Three days later, the QRS complex had changed markedly in Lead III (Fig. 3,*C*). The Q-S_3 deflection had been replaced by a small R wave and a large S deflection, and the axis was now strongly toward the left. At this time there was an inverted T_1 deflection of the coronary type with a slightly inverted T_2 wave, and in Lead III a normal S-T junction with an upward T wave. The precordial lead showed a large Q wave, a well-developed R deflection, a slightly elevated S-T junction, and an inverted T wave. Four later records, the last of which was obtained four days before death (Fig. 3,*D*), showed essentially similar features. In the healing stage, the record in the limb leads resembles the



A. *B.* *C.* *D.*

Fig. 3 (Case 4).—*A*, Record before infarction. *B*, Record on the day of the attack. *C*, Record on the third day after the attack. *D*, Record on the sixteenth day after the attack.

picture in anterior infarction, but there is also some resemblance to the pattern associated with hypertrophy and left ventricular strain. In the precordial lead, the picture is typical of the healing stage of anterior infarction. In the acute stage, the record did not suggest a diagnosis of anterior infarction.

In Case 5 there was an infarct which involved only the anterior portion of the septum, coming to the surface beneath the endocardium in the left ven-

tricle and somewhat in the right ventricle but the anterior wall or the epicardial surface of the heart was not reached. In spite of the lack of epicardial involvement, the record of the acute stage (Fig. 2,*A*) failed to show the R wave in the precordial lead, where a large Q-S deflection and typical elevation of the S-T junction were present. In the limb leads the appearance was not characteristic of an acute infarct but showed an isoelectric T_1 wave and a depression of the S-T segment with upward T waves in Leads II and III, an appearance like that induced by exercise and by anoxemia in susceptible hearts. In this case the record as a whole was diagnostic of acute infarction only because of the absence of the R wave and the characteristic appearance of the S-T and T deflections in Lead IVF.

It is of especial interest that, with this purely septal infarct, there is a Q-S deflection—absence of the R wave—in the precordial lead, such as has been attributed to damage of the whole thickness of the anterior wall of the ventricle,[1] and that the T wave in this lead had the appearance supposed to result from damage to the superficial anterior layers of the myocardium.

Of the three cases with incomplete anterior wall infarction with septal involvement, Cases 2 and 5 had a Q-S deflection in the precordial lead, as would have been expected with a lesion involving the whole thickness of the anterior wall, and the T wave had the appearance expected with necrosis of the superficial anterior layers of the myocardium. Case 4 showed normal R and S waves in Lead IV of the early record, but the later record showed a large Q wave followed by R and S deflections as would be expected in a heart such as this with remaining viable subepicardial fibers above necrosis reaching to the endocardium.[2] The early record had the S-T and T deflections of Lead IV opposite in direction to what would have been expected with an acute anterior infarction, but the later records in this lead were typical of anterior infarction in the healing stage. Case 2 alone showed the classical pattern of anterior infarction in both limb leads and precordial leads. Cases 3, 4, and 5 showed S-T- and T-wave abnormalities in the limb leads of the earliest records like those commonly seen after exercise and anoxemia tests. The precordial lead in the first of these cases was normal; in the second it resembled that seen with exercise and anoxemia tests; and, in the third, it suggested anterior infarction.

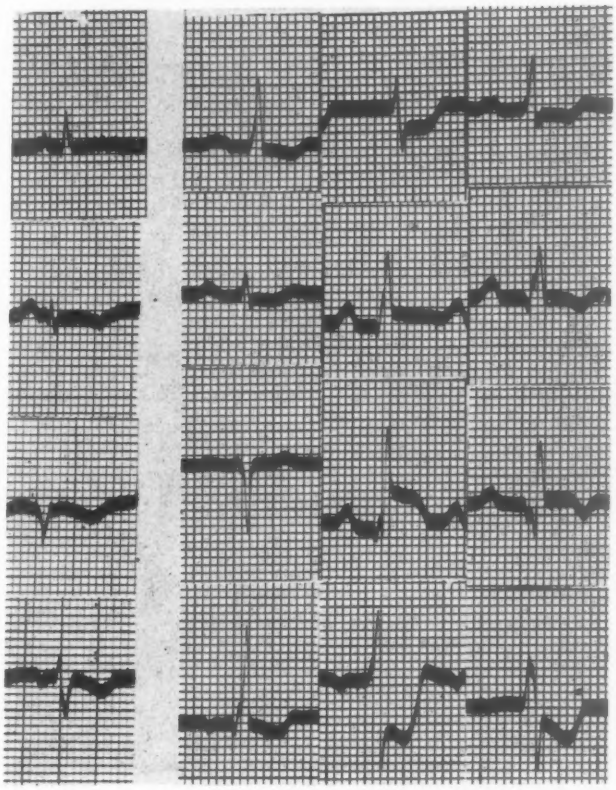
There was one recent lateral wall infarct (Case 6) which extended into the posterior wall and showed S-T- and T-wave changes like those associated by Wolferth and his associates[7] with the acute stage of lateral infarction. Case 7 showed an old healed lateral infarct with the inverted T_1 and T_4 waves, and preservation of the R_4 wave which would be expected according to Wolferth's descriptions.

There were five cases with a typical posterior, i.e., diaphragmatic, situation of the infarct, two (Cases 10 and 11) with, and three (Cases 8, 9, and 12) without septal involvement. Three of these cases (Cases 9, 10, and 11) afforded an opportunity to observe the effect of the infarct upon the electrical axis of the QRS complex. A comparison of the records, before and after infarction (compare Figs. 4,*B* and C, and 5,*A* and B), showed that, in all three, the electrical axis of the QRS complex was rotated toward the right, though it still remained within the normal sector.

Cases 8, 10, and 11 each had an infarct involving the complete thickness of the posterior wall and all had a large Q_3 wave.

The records of Cases 10 and 11, with complete posterior wall and septal involvement, showed a large Q_3 wave and the typical acute S-T- and T-wave

changes associated with posterior infarction, with marked elevation of the S-T junction in Lead III and depression of the S-T junction in Leads I and IV. Case 11 (Fig. 4,*C* and *D*) showed a total inversion of the T wave in Lead IV which is not ordinarily described as a feature of posterior infarction. Case 8 (Fig. 4,*A*), with a complete mural lesion without septal involvement, showed the S-T junction and the T waves in Leads II and III of the subacute or healing type (coronary T waves), but it must be borne in mind that the record was not obtained until five days after the attack occurred. An earlier record might have shown more typical acute S-T- and T-wave changes. The precordial lead had negative S-T and T deflections of a nonspecific appearance, somewhat like the later record of Case 11 (Fig. 4,*D*).

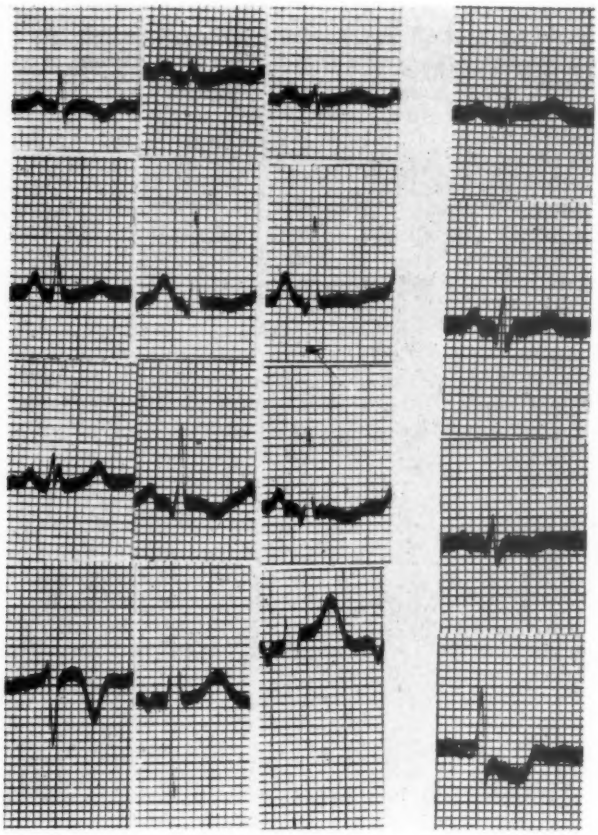


A. *B.* *C.* *D.*

Fig. 4 (Case 8).—*A*, On the fifth day after infarction. *B*, (Case 11), Before the infarction. *C*, On the day of the attack. *D*, On the second day after the attack.

There were two cases with an incomplete posterior wall lesion (Cases 9 and 12). Case 9 showed recent subendocardial and posterior wall necrosis, without involvement of the subepicardial layers or septum, and an old anterior septal scar. The record before the infarction (Fig. 5,*A*) showed T-wave changes due to the old anterior lesion. The record taken the day after the infarct (Fig. 5,*B*) showed in the limb leads a small Q_3 deflection and a minimal elevation of the S-T_3 junction, while in Lead II there was a suggestion of the coronary T wave usually associated with the healing stage of infarction. The precordial lead developed a small R′ wave but had a normal appearance of the S-T segment and T wave, although the S-T segment was at a lower level than before the infarct. In later records the coronary T_2 wave persisted, the S-T junction returned to the zero level in Lead III, and to slightly above it in

Lead IV (Fig. 5,*C*). The absence of a large Q_3 wave in this case might be ascribed to the fact that the old area of degeneration in the anterior part of the septum had prevented the development of a large Q_3 deflection by removing the potentials normally supplied by this area. The S-T- and T-wave changes in the limb leads were fairly typical of those due to posterior infarction, though not especially suggesting an acute lesion.



A. *B.* *C.* *D.*

Fig. 5 (Case 9).—*A*, Before the infarction. *B*, On the first day after the attack. *C*, On the fifth day after the attack. *D*, (Case 12), on the eighth day after infarction.

Case 12 had a large intramural posterior wall infarct with only very small areas of subepicardial and subendocardial involvement, each about 4 by 8 millimeters. The record (Fig. 5,*D*), taken two days after the infarction, revealed nothing characteristic of the infarct picture in the limb leads while the precordial lead showed marked negativity of the S-T segment and of the T wave, as is occasionally seen after posterior infarction associated with typical limb lead patterns (e.g., Fig. 4,*D*). Such a T_4 wave is also seen associated with the limb lead features of the exercise reaction. In Case 12, however, without typical limb lead patterns, the appearance of Lead IV is not suggestive of acute infarction. In the limb leads there is a very slight elevation of the S-T junction in Lead I and a slight depression of this part of the curve in Lead III. The amplitude of these deflections is very small. This deflection is in the opposite direction to what one would expect from an acute posterior wall lesion.

DISCUSSION

A careful study of the site and extent of the infarct and a correlation of this with the QRS-, S-T-, and T-wave changes in twelve cases have revealed certain features that are worthy of emphasis:

Of six cases with records before and after infarction, there were three cases with an anterior lesion. One showed a shift of the axis of the QRS complex toward the right; one showed no shift of the axis; and the other showed a shift toward the left. There were three cases with a posterior lesion, and all three showed a shift of the axis of the QRS complex toward the right.

Of two anterior wall infarcts with septal involvement (Cases 2 and 5), one was associated with typical acute S-T-changes in the limb leads and in the precordial lead and both with the typical Q-S deflection in the precordial lead. A Q-S deflection in the precordial lead would not have been expected in either of these cases because the heart did not show involvement of the subepicardial fibers, the feature that has been supposed to give rise to this change in the record.

The importance of necrosis of the anterior part of the septum in relation to changes in the precordial lead is further indicated by the fact that the one case of anterior infarction without such septal involvement (Case 3) failed to show any abnormal features in this lead, while the other four cases of anterior infarction did have septal involvement and were associated, either early or later, with the QRS-, S-T-, and T-wave changes in Lead IV, considered typical of anterior infarction.

Of the four anterior infarcts without subepicardial necrosis, only one (Case 2) was associated with the typical QRS-, S-T-, and T-wave changes of acute anterior infarction in both limb leads and precordial lead. Case 5 showed typical acute changes in the precordial lead alone. Case 4 showed a peculiar appearance in the first record but in the records of the third day after infarction and later both limb leads and precordial lead suggested anterior infarction. Case 3 was not typical of infarction in the limb leads, and the precordial lead was normal. Cases 3, 4, and 5 showed S-T- and T-wave changes in the limb leads of the early records like those seen after exercise and anoxemia tests.

There were two complete posterior wall infarcts with septal involvement (Cases 10 and 11) and these had typical acute S-T- and T-wave changes in both limb leads and precordial lead. There was one complete posterior wall infarct without septal involvement (Case 8) and on the fifth day after the attack this case showed S-T- and T-wave changes in the limb leads like those associated with a healing posterior infarct. The precordial lead had a depressed S-T segment and an inverted T wave, unlike the usual appearance in the healing stage of posterior infarction.

Two cases with posterior wall infarction without subepicardial involvement and also without septal involvement (Cases 9 and 12) failed to show typical acute S-T- and T-wave changes in the limb leads. In the precordial lead of Case 9 there was a normal S-T segment and T wave, and, in that of Case 12, the S-T segment and T wave resembled the usual exercise test pattern, though of a type occasionally accompanying the typical limb lead pattern of acute posterior infarction.

A lesion of either anterior or posterior wall, involving also a part of the adjacent septum, occurred five times (Cases 1, 2, 4, 10 and 11). It was associated, except in Case 4, with the typical S-T- and T-wave changes of the acute phase of the infarction curve both in the limb leads and the precordial lead. The

changes were of the anterior or the posterior type, in conformity with the mural involvement. Mural necrosis without septal involvement occurred in four cases, none of which had the typical S-T- and T-wave changes of acute infarction (Cases 3, 8, 9, and 12). In the five cases with posterior lesions, typical acute S-T- and T-wave changes, both in limb leads and in the precordial lead, were found only in the presence of complete transmural and posterior septal involvement (Cases 10 and 11). In the five with anterior lesions, typical acute S-T- and T-wave changes were found both in limb leads and in the precordial lead in only two cases (Cases 1 and 2). Both of these had septal involvement, one with complete transmural necrosis, the other with incomplete involvement of the wall, lacking necrosis of the subepicardial layers.

The importance of involvement of the septal muscle in relation to the appearance of the acute S-T-segment changes of infarction in both the anterior and posterior situations is surprising, for it has been our opinion that damage to the subepicardial muscle caused the typical S-T elevation.

A Q-S_4 deflection occurred once with involvement of the septum and entire thickness of the anterior wall (Case 1), once with anterior wall and septal involvement without the epicardial surface apparently being affected (Case 2), and once with only the septum and the endocardial surface showing damage (Case 5). One would expect involvement of the whole anterior wall to accompany the appearance of the Q-S_4 deflection, but in these cases the only constant pathologic feature is necrosis of the anterior part of the septum and subendocardial layers. A large Q_4 wave with an R and S deflection was found in the later records of Case 4, as would have been expected with the deeper layers of the anterior wall affected, without subepicardial degeneration. These waves, however, did not appear in Case 2 which showed a similar pathologic appearance. The apparent importance of the septal muscle in relation to the appearance of a Q-S_4 deflection is surprising in view of our belief that a lesion affecting the whole depth of the anterior wall is necessary to abolish the preintrinsic R deflection. What has been said previously about the lack of relationship between the structural appearance of heart muscle and its ability to produce a normal electrical curve must be recalled in relation to the disappearance of the R deflection from the precordial lead. It is possible that apparently intact muscle fibers might fail to give a normal electrical reaction, but it is noteworthy that in Case 5 the necrotic area did not involve any part of the anterior wall of either ventricle. It would seem surprising that a physiologic change would extend so far from the necrotic area that was found.

A large Q_3 deflection occurred twice with a complete lesion of the posterior wall and septum (Cases 10 and 11) and once with a complete posterior wall lesion but without the septal involvement (Case 8). A small Q_3 deflection appeared once with an incomplete posterior wall lesion, without the epicardial surface and the septum, but there was also marked old scarring of the anterior septum, which might have prevented the appearance of a wave of larger size. Complete transmural involvement of the posterior wall was the only constant pathologic finding in the cases with a large Q_3 deflection. A large Q_3 deflection, previously present, was twice abolished by an infarct of the anterior wall, once occurring with, and once without, septal involvement.

The apparent dependence of the Q_3 deflection upon posterior mural lesions, rather than upon posterior septal lesions is of interest. The abolition of a Q_3 deflection, previously present, by a recent intramural infarct in the anterior wall, without septal involvement, also has an important bearing upon our concept of the genesis of the Q_3 deflection. It indicates that the muscle of the anterior

wall has a part in the appearance of the Q_3 deflection in cases with posterior infarction, a fact sometimes lost sight of in theoretical discussions of the cause of this wave.

The resemblance of the limb leads of Cases 3, 4, and 5, with anterior infarction without subepicardial involvement to those records seen after anginal attacks, exercise tests, and anoxemia tests is of interest. The reason for the similarity of these records may be that in both types of cases there is a limitation of the necrosis, on the one hand, and the ischemia, on the other, to the subendocardial and intramural layers of the wall. That cases of angina may have lesions of this character has been demonstrated by Büchner,[8] who found areas of subendocardial necrosis in patients dying after attacks of anginal pain without the typical clinical features of infarction, such as fever, leucocytosis, and increased sedimentation rate. Case 12, with an incomplete posterior lesion, showed T-wave changes of this type in the precordial lead alone.

It is a striking fact that the incomplete mural infarcts, without involvement of the subepicardial layers of the ventricular wall, rarely have records that definitely resemble the typical acute infarction curve of anterior or posterior type. In only one of the six cases (Case 2) was the record typical of such a diagnosis. In Case 5, the precordial lead made the diagnosis probable, and, in Case 4, the first record suggested an acute lateral infarct. In Cases 3, 9, and 12, neither the limb leads nor the precordial lead suggested acute infarction.

There is no definite pattern by which these incomplete mural infarcts can be recognized, for Case 2 demonstrates that they may even give rise to a typical infarction record, but the frequency of S-T- and T-wave patterns like those appearing after exercise and anoxemia tests is worth stressing and also that these patterns may be found in either the limb leads or in Lead IVF, but rarely in both.

One case of acute lateral infarction was observed to have the electrocardiographic appearance described by Wolferth, as was also a case with an old healed lateral infarction.

A search of the literature reveals but three autopsied cases comparable to those of our series and with an electrocardiogram including Lead IV. Langendorf and Kovitz[9] reported two cases of anterior infarction without the subepicardial layers being necrotic and with septal involvement. Neither of these cases had records suggesting acute infarction. One of them showed in the limb leads a normal S-T junction, an upward T_1 deflection, and inverted T_2 and T_3 deflections with low voltage. In Lead CF_2 there was a large Q-S deflection, and a normal S-T segment and T wave, while in Lead CF_4, the R wave was present, the S-T segment was normal, and the T wave was coved and inverted. The other case showed a typical exercise pattern in the limb leads with depressed $S\text{-}T_1$ and $S\text{-}T_2$ segments and upward T waves. Lead CF_2 was normal and CF_4 had a normal R wave and normal S-T junction but an inverted T wave. Price and Jams[10] reported a case with posterior infarction involving only the subendocardial layers of the posterior wall and septum and "extending on to the anterior wall of the left ventricle in its middle and apical portions. This anterior portion gradually left the subendocardial layers to become intramural near the apex." The record of this case resembled those of the healing stage of posterior infarction (e.g., Fig. 4,*D*). The limb leads showed minimal S-T depression in Lead I with an upward T deflection; the T_2 wave was coved and inverted; the $S\text{-}T_3$ junction was +0.5 mm., and the T_3 deflec-

tion was inverted. A large Q_3 deflection was present. Lead IVR showed a normal R wave, a normal S-T segment, and an inverted T wave.

The findings in these three cases are at variance with ours in that the two anterior infarcts with septal involvement, without necrosis of the subepicardial layers of the anterior wall, did not have a Q-S deflection in Lead IV. One of our cases, in fact, did not show this in the early record but did have a large Q_4 wave in later ones. Disagreement was also found in the case with posterior infarction without a complete transmural lesion, which, nevertheless, had a large Q_3 deflection. They were in agreement with our findings in that one of the anterior cases had the appearance in the limb leads commonly seen after exercise and anoxemia tests and that all three lacked subepicardial necrosis and failed to show the typical electrocardiographic features of acute infarction.

SUMMARY AND CONCLUSIONS

It is difficult to summarize these observations because of the many electrocardiographic features that must be considered. Certain associations have appeared definite enough to warrant emphasis, in spite of the small number of cases. In this connection, however, the relation between the structural integrity of the myocardium and its ability to produce a normal electrical curve must be considered. There may be a depression of the physiologic activity of muscle without either gross or microscopic anatomic changes but, as far as structural alterations are concerned, the following conclusions seem justifiable:

After either anterior or posterior infarction, but more uniformly after the latter, there is a rotation of the electrical axis of the QRS complex toward the right.

The typical S-T- and T-wave changes, that we have come to associate with acute infarction, occur most often in the presence of necrosis of the anterior or posterior wall, including a portion of the adjacent interventricular septum. Mural necrosis without septal involvement may be associated with these typical changes, but not as constantly.

The typical S-T- and T-wave changes in the limb leads and the precordial lead, and the Q-S deflection in the precordial lead, occasionally appear after anterior infarction, even without necrosis of the subepicardial layers of the wall.

The Q-S or Q deflection in the precordial lead is associated with necrosis of the anterior part of the septum and may be present when this part of the septum is affected, even without involvement of the anterior wall.

A large Q_3 deflection may appear without the presence of necrosis in the posterior part of the interventricular septum, if there is a complete transmural lesion.

The records of cases with anterior infarction without subepicardial necrosis somewhat resemble those seen after exercise and anoxemia tests and during anginal attacks.

The records, after either anterior or posterior infarction without involvement of the subepicardial layers of the wall, rarely have an appearance that closely resembles the typical acute infarction curve of anterior or posterior type.

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TRANSIENT "0" DIASTOLIC BRACHIAL PRESSURE (INDIRECT), ASSOCIATED WITH NORMAL OR ELEVATED POPLITEAL PRESSURE, TACHYCARDIA, AND NERVOUS TENSION

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IN THE course of the routine examinations of men between the ages of 18 and 45 years for induction into the Armed Forces* of the United States, a cardiovascular syndrome, hitherto undescribed, was observed in thirty-eight examinees exhibiting a pronounced degree of nervous tension. In addition to the nervous element, the syndrome was characterized by transient "0" diastolic brachial pressure (indirect method), normal or elevated popliteal pressure, and tachycardia.

In the initial cases it was felt that perhaps we were observing instances of functional aortic insufficiency (despite certain features to the contrary to be mentioned later); consequently blood pressure readings were recorded in the lower extremities. The desirability of these latter determinations was based on the observations of Hill, Flack, and Holtzmann,[1] Hill and Rowlands,[2] and Loewenberg[3] who have reported the occurrence, in organic aortic insufficiency, of a more pronounced discrepancy between the brachial systolic pressure and the popliteal systolic pressure than occurs physiologically[4] (Hill's sign[5, a]). Loewenberg[3] has recently stressed the importance of this sign in distinguishing functional from organic aortic insufficiency. Unfortunately, several earlier cases observed are not included in this report inasmuch as the significance of the

These observations were made during the period in which the author served as cardiologist on the Examining Board of the Armed Forces Induction Station, Tacoma and Seattle, Washington.
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*All branches of service; the majority represent examinations for induction into the Army.

observations was not clear at the time, and no detailed data were recorded. It was not until several instances had been encountered that we were prompted to perform more complete studies. Inasmuch as no reference to this syndrome could be found in the literature, the observations are reported.

PROCEDURE

Brachial arterial pressure was determined* by the indirect method in the antecubital space; a standard mercury manometer with a cloth covered, 13-cm. (width) rubber cuff, hook-on type, was employed. The examinee was in the sitting position, with his arm slightly flexed and with his forearm at the level of the heart. Readings were recorded by the auscultatory method in accordance with the recommendations of the Committees for the Standardization of Blood Pressure Readings of the American Heart Association and of the Cardiac Society of Great Britain and Ireland.[6] The routine procedure was to record the level of the diastolic pressure at a well-defined fourth phase (muffling of the sounds), or, if absent, at the fifth phase (disappearance of the sounds). None of the examinees included in this report exhibited a clear, definite transition, although in several instances a faint change was audible. In this regard it might be mentioned that considerable uncertainty still exists as to which of the two phases is the more reliable index of diastolic pressure.[7, 8] The popliteal blood pressure was determined in a similar manner in the popliteal fossa; readings were recorded both in the standing and prone positions in all examinees exhibiting a diastolic brachial pressure of "0." The cuff was the same as that employed in the upper extremity. Circumstances precluded the use of a wider cuff. It is doubtful, however, with the employment of a cuff lined with metal ribs and a hook-on device which prevented slipping or bulging of the rubber sac, if this factor could have exerted any significant influence on our basic observations.[4] Each examinee was completely naked, and the examining room was kept at a comfortable temperature level. No physical effort preceded the blood pressure determinations for at least thirty minutes other than the effort of undressing and that associated with a gradual, short move in line. The examinations were conducted in the morning and early afternoon. In the majority of instances, there was no food intake for several hours preceding the examinations. The brachial blood pressure determinations were part of the routine induction examination. The popliteal examination was performed when the brachial diastolic pressure was recorded as "0." An examinee exhibiting a brachial diastolic pressure of "0" was reassured, encouraged to relax and given a rest period (seated) of from five to fifteen minutes. Then the blood pressure readings were repeated. If still unchanged, he was told to resume his seat, and the readings were repeated at ten- to twenty-minute intervals generally, until the brachial diastolic pressure had attained a level of 60 mm. Hg or over. One case was observed in which a normal brachial diastolic level was not attained at the end of one and three-fourths hours. This examinee was in a state of marked nervous tension, and although circumstances prevented a longer rest period, it was felt, after complete cardiac studies, that this case represented a similar example of the phenomenon described. This man is not included in the group reported. Blood pressure determinations were frequently repeated in the contralateral arm and leg.

*Routine blood pressure determinations were performed by trained Medical Department enlisted men, instructed in the errors of technique, who referred all examinees exhibiting this phenomenon to the author for repeat readings and cardiovascular studies.

RESULTS

Thirty-eight examinees exhibited a relatively uniform pattern, the outstanding feature of which was a "0" brachial diastolic pressure, transitory in nature. The data are presented in Table I. The brachial systolic pressure on initial examination ranged from 118 to 250 mm. Hg, and averaged 159.1. The popliteal systolic pressure in the prone position ranged from 162 to 300 mm. Hg; the average was 202.3. The popliteal diastolic pressure in the prone position ranged from 68 to 144 mm. Hg, and averaged 101.9. In the standing position, the popliteal systolic pressure ranged from 190 mm. Hg (the only reading below 200) to 300 mm. Hg, the latter noted in six men; the average was 247.3. The diastolic pressure in the popliteal artery in the standing position ranged from 98 to 246 mm. Hg; the average was 159.7. The lowest prerest heart rate noted was 90; only two were below 100. The highest rate was 168. The average was 127.4. The heart rate was determined in the sitting position. Rest periods necessary to bring about return of the brachial diastolic pressure to 60 mm. Hg or above (exclusive of the examinee mentioned previously who did not exhibit a return to normal at the end of one and three-fourths hours) ranged from five to ninety minutes, and averaged 25.8 minutes. Detailed data, together with the changes in these values associated with the return of the brachial diastolic pressure readings to values of 60 mm. Hg or over, are presented in Tables I, II, and III.

Four groups of examinees could be delineated (Table I): Group 1, which includes Cases 1 through 13, represents those men whose brachial systolic pressure, before rest, did not exceed 140 mm. Hg and whose brachial systolic and diastolic pressures after rest did not exceed 140 and 90 mm. Hg, respectively. This group probably can be safely eliminated as being nonhypertensive. Group 2 includes Cases 14 through 18 (five men) and represents those men whose prerest or postrest systolic brachial pressure exceeded 140 mm. Hg but did not exceed 150, and whose post-rest brachial diastolic pressure did not exceed 90. The inclusion of this as a separate group is made because of the existing uncertainty as to the blood pressure levels constituting hypertension.[9] The United States Army[10] employs 150 mm. Hg, systolic, and/or 90 mm. Hg, diastolic, as the upper limits of normal for inductees. Others regard 140 mm. Hg and/or 90 mm. Hg, systolic and diastolic, respectively, as the upper limits of normal. Group 3 includes Cases 19 through 27 (nine men) and incorporates those examinees whose postrest brachial systolic and diastolic pressures did not exceed 140 and 90 mm. Hg, respectively, but whose prerest brachial systolic pressure exceeded 150. Group 4 includes Cases 28 through 38 (eleven men) who exhibited postrest brachial readings exceeding 150 mm. Hg, systolic, and/or exceeding 90 mm. Hg, diastolic. The postrest brachial pressure, that is, the blood pressure following recovery of the diastolic pressure to normal levels, is used as the principal basis for the delineation of the cases into four groups inasmuch as it is obvious that it represents a closer approximation to the actual blood pressure than does the initial (prerest) reading.

It is interesting that following rest only two examinees revealed a brachial diastolic pressure exceeding 90 mm. Hg (although three were observed to reach this level), and in view of the frequency with which blood pressure lability was previously observed in Army[9] and Navy[11] examinees, and the evident nervous state of these men, it is exceedingly questionable if the majority of the examinees in Group 4 can be classed as having true hypertension. The influence of other factors on normal arterial pressure has been elaborated repeatedly.[9, 12-15]

TABLE I. DATA ON THE EXAMINEES EXHIBITING THE SYNDROME

NAME	AGE (YRS.)	INITIAL READINGS				REST (MIN.)	READINGS AFTER REST PERIOD				"PERIPHERAL PHENOMENA"							
		BRACH. B.P.	POPLITEAL B.P.		HEAR RATE*		BRACH. B.P.	POPLITEAL B.P.		HEART RATE*	CAPILLARY PULSATION		"CORRIGAN PULSE"		"PISTOL-SHOT" SOUND		DUROZIEZ' MURMUR	
		SITTING	PRONE	STANDING			SITTING	PRONE	STANDING		BEFORE REST	AFTER REST	BEFORE REST	AFTER REST	BEFORE REST	AFTER REST	BEFORE REST	AFTER REST
Group 1																		
1. L. K.	38	130/0	176/ 96	220/118	122	25	134/75	168/ 86	210/108	80	–	–	–	–	+	–	–	–
2. R. L.	23	128/0	164/ 72	200/130	120	45	138/68	165/ 78	208/132	108	–	–	–	–	–	–	–	–
3. G. W.	20	140/0	196/100	220/170	142	20	136/84	190/ 94	218/194	112	–	–	+	–	+	–	–	–
4. P. L.	20	132/0	175/ 90	226/148	108	5	138/65	174/ 92	220/142	94	–	–	–	–	–	–	–	–
5. P. S.	20	120/0	168/ 86	218/124	104	15	120/60	160/ 82	212/118	100	–	–	–	–	–	–	–	–
6. R. M.	20	128/0	162/ 98	190/142	136	30	122/62	145/ 76	170/126	104	–	–	–	–	+	–	–	–
7. J. M.	21	118/0	170/100	210/140	126	10	116/65	168/ 90	200/140	110	–	–	–	–	–	–	–	–
8. W. L.	18	140/0	200/106	255/180	90	10	128/76	180/100	240/180	76	–	–	–	–	–	–	–	–
9. A. M.	23	138/0	165/ 96	200/140	122	25	138/70	154/ 90	190/140	104	–	–	–	–	–	–	–	–
10. R. L.	20	130/0	198/115	300/195	100	20	130/75	170/105	300/190	100	–	–	–	–	–	–	–	–
11. G. E.	23	138/0	170/ 90	204/122	120	5	140/66	165/ 82	196/115	92	–	–	–	–	+	+	–	–
12. A. J.	28	140/0	185/100	250/180	138	20	140/65	172/ 85	245/164	128	–	–	–	–	–	–	–	–
13. H. L.	30	135/0	182/ 80	230/124	126	30	130/70	176/ 85	218/130	104	–	–	–	–	–	–	–	–
Group 2																		
14. A. M.	29	136/0	178/ 94	208/140	114	40	142/84	175/ 96	200/134	90	–	–	+	–	+	–	–	–
15. R. F.	21	142/0	188/102	220/126	106	25	128/62	170/ 94	205/114	82	–	–	–	–	+	–	–	–
16. A. S.	20	148/0	186/ 98	238/192	160	30	130/74	170/ 95	220/190	148	–	–	–	–	–	–	–	–
17. E. S.	22	148/0	180/ 95	234/125	144	30	140/78	176/ 90	218/120	96	–	–	–	–	–	–	–	–
18. A. H.	22	150/0	186/100	234/132	112	15	148/70	170/ 94	206/118	88	+	–	+	–	+	–	–	–
Group 3																		
19. R. Y.	21	154/0	186/ 88	230/144	168	35	146/60	184/ 88	222/130	98	–	–	–	–	–	–	–	–
20. J. B.	27	160/0	208/114	245/136	142	35	140/90	186/ 96	228/124	130	–	–	–	–	–	–	–	–
21. G. B.	21	160/0	200/112	298/212	124	35	140/60	200/108	294/210	106	+	–	+	–	+	+	–	–
22. T. R.	18	160/0	225/105	278/188	152	90	150/76	218/102	256/180	108	–	–	–	–	–	–	–	–
23. G. N.	19	162/0	200/ 68	260/132	100	30	130/64	190/ 68	244/130	86	–	–	–	–	–	–	–	–
24. J. K.	19	170/0	204/ 90	248/168	130	15	148/60	200/ 90	230/160	108	–	–	–	–	+	–	–	–
25. H. G.	20	174/0	188/ 98	262/192	158	20	150/90	178/ 90	250/192	124	–	–	–	–	–	–	–	–
26. R. D.	19	190/0	220/ 98	265/175	92	5	150/70	206/ 90	250/168	84	–	–	–	–	–	–	–	–
27. E. W.	19	210/0	274/112	300/165	132	10	150/84	226/105	282/140	100	–	–	–	–	–	–	–	–
Group 4																		
28. C. G.	21	168/0	210/104	266/125	148	35	152/68	204/ 98	254/116	102	–	–	–	–	–	–	–	–
29. J. D.	21	174/0	196/ 98	222/170	130	15	154/72	188/ 90	220/145	118	–	–	–	–	+	–	–	–
30. A. E.	28	170/0	218/ 96	274/210	136	5	160/88	200/ 84	250/198	130	–	–	–	–	–	–	–	–
31. J. W.	35	188/0	216/124	240/170	104	5	168/74	195/100	210/160	98	–	–	–	–	+	–	–	–
32. T. P.	27	190/0	272/135	300/230	144	55	170/85	216/114	280/186	112	–	–	–	–	–	–	–	–
33. R. S.	19	152/0	180/ 84	214/ 98	128	85	172/80	200/ 92	236/104	112	–	–	–	–	–	–	–	–
34. R. K.	23	190/0	245/130	300/190	148	15	175/85	215/115	290/184	130	–	–	–	–	+	–	–	–
35. L. M.	20	148/0	195/102	250/144	130	15	180/80	198/104	266/174	100	–	–	–	–	–	–	–	–
36. M. J.	27	200/0	252/126	288/176	114	25	170/90	214/110	272/170	102	–	–	+	–	+	–	–	–
37. N. M.	29	235/0	270/128	300/175	140	10	206/100	270/124	300/168	120	–	–	–	–	+	–	–	–
38. W. L.	35	250/0	300/144	300/246	132	40	220/112	278/120	300/210	96	–	–	–	–	+	–	–	–

*Sitting heart rate.
+ represents presence.
– represents absence.
See text for comment on systolic pressure readings of 300 mm. of mercury.

Cases 37 and 38 are probably the only examinees who can be justifiably regarded as hypertensive, and yet blood pressure readings of such levels have previously been demonstrated[9] to occur transiently in hyperexcitable Army inductees with markedly labile vasomotor mechanisms. For this reason these groups have all been incorporated, as subdivisions, in one table rather than tabulated separately. None of the examinees, including Examinees 37 and 38, were demonstrated to have organic heart disease following complete studies.

TABLE II. DIRECT COMPARISON BETWEEN INITIAL (PREREST) AND POSTREST READINGS

	BRACHIAL B.P. (MM. HG)		POPLITEAL B.P. (MM. HG)				
	SITTING		PRONE		STANDING		HEART
	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC	RATE†
Initial (prerest) readings:							
Lowest	118	"0"	162	68	190	98	90
Highest	250	"0"	300‡	144	300‡	246	168
Average	159.1	"0"	202.3	101.9	247.3	159.7	127.4
Postrest readings:							
Lowest	116	60	145	68	170	104	76
Highest	220	112	278	124	300‡	210	148
Average	148.1	75.2	189.8	94.8	237.1	152.6	104.7
Average change* from prerest to postrest values	-11.0	+75.2	-12.5	-7.1	-10.2	-7.1	-22.7

*– represents decrease.
+ represents increase.
†Sitting heart rate.
‡Maximum value obtainable with mercury manometer employed.

TABLE III. RESPONSE OF EXAMINEES TO RISE OF THE DIASTOLIC PRESSURE FROM "0" TO 60 MM. HG OR ABOVE

	BRACHIAL SYSTOLIC PRESSURE (SITTING)	POPLITEAL B.P.				HEART RATE*
		PRONE		STANDING		
		SYST.	DIAST.	SYST.	DIAST.	
Number of examinees exhibiting:						
Decrease	27	33	29	32	29	37
No change	4	2	3	3	4	1
Increase	7	3	6	3	5	0

*Sitting heart rate.

It might be well to mention, at this point, that 300 mm. Hg was the highest value obtainable with the mercury manometer employed. However, inasmuch as the number of these readings was small, and the probability that the unknown excess was not great, it is unlikely that the averages cited are altered to any significant degree. In any event it is evident that they could have little effect upon the basic observations.

"Peripheral phenomena" (Lewis) exhibited considerable variability (Table I). The most common was the "pistol-shot" sound, occurring in fifteen examinees; in all but two instances they disappeared following return of the brachial diastolic pressure to normal. Next in frequency was the Corrigan pulse, observed in five men. Capillary pulsation was clinically demonstrable in only two instances. Both the Corrigan pulse and capillary pulsation disappeared following return of the brachial diastolic pressure to normal. Duroziez' murmur was not encountered.

TABLE IV. AGE DISTRIBUTION OF EXAMINEES*

AGE (YRS.)	18 TO 20	21 TO 25	26 TO 30	31 TO 35	36 TO 40	41 TO 45
NUMBER OF CASES	15	12	8	2	1	0

*See text for comment on relation to general age groups represented by total examinees.

See text for comment on systolic pressure readings of 300 mm. of mercury.

It will be noted in Table IV that the vast majority of the examinees exhibiting the syndrome were in the younger age groups. There were fifteen between 18 and 20 years of age, twelve between 21 and 25, eight between 26 and 30, two between 31 and 35, one between 36 and 40, and none between 41 and 45 years of age. This proportion far exceeds the general age proportions represented by the examinees, and seems to indicate a predilection for younger persons. A direct comparison with the precise age proportions of the total number of examinees cannot be given for military reasons.

DISCUSSION

The return of the diastolic brachial pressure from "0" to normal or above occurred relatively rapidly in the majority of the examinees. In several instances the sounds were observed to appear and disappear while the cuff remained deflated and the mercury maintained at "0" level, or while the examinees rested with no cuff applied to the arm and with care exercised to avoid compression of the brachial artery with the diaphragm of the stethoscope. It should be recalled that these men were completely undressed, and an arterial constrictive factor was thus eliminated. In some cases a gradual climb in diastolic brachial pressure was noted as manifested by readings obtained on repeated determinations. The length of time required for the "0" diastolic pressure to return to 60 mm. Hg or more appeared to bear no direct relationship to either the cardiac rate or the height of the systolic pressure associated with the "0" diastolic pressure.

The mechanisms involved in the genesis of the syndrome are difficult to explain. Katz[16] suggests this phenomenon may resemble that which arises occasionally in the upper extremities in free aortic regurgitation in which a systolic murmur and thrill occur in these extremities when they are raised above the head. He feels that in our examinees, either through autonomic (nervous) effects or epinephrine release, the result of fear and excitement, stroke output is increased and peripheral vasodilatation occurs. The effect of the inadequately filled vessels and high pulse pressure is to create sufficient turbulence, as the anacrotus becomes steeper approaching the periphery, to produce audible brachial vibrations despite the existence of zero pressure in the blood pressure cuff.

An interesting hypothesis which merits consideration is the operation of an adrenergic mechanism based upon Cannon's[17, 18] theory of epinephrine release in fear. Goodman and Gilman[19] state that, apparently, when epinephrine is absorbed slowly, as from hypodermic injection, vasodilatation occurs in the skeletal muscles. This has been demonstrated by Blumgart,[20] Starr and his associates,[21] and others.[22-25] It would be presumed that the nervous tension exhibited by the examinees was an expression of fear, which, stimulated, increased adrenal activity; this resulted in the release of small amounts of epinephrine into the circulation, producing arterial dilatation in the muscle bed of the upper extremities and initiating certain compensatory reflex mechanisms which maintain normal vascular tone or bring about vasoconstriction in the lower extremities, to counteract the effects of the vasodilatation in the upper extremities in order that physiologic blood pressure levels and adequate cerebral flow be maintained. There also appears to be evidence suggesting that, under certain conditions, the lower extremities may be more responsive to vasoconstrictor influences than the upper extremities. Downman and his associates,[26] employing decerebrate and anesthetized cats, in the horizontal position, have recently observed that in some of the animals various sensory stimuli brought about reflex

vasoconstriction in the paws of both the hind legs and the forelegs, but in others the vasoconstrictor response was confined to the paws of the hind legs only. They regard the anatomic plan of the reflex as the same in man. Evans and Stewart[27] have noted a more pronounced degree of reduction in the skin temperature of the foot than of the hand as a result of smoking, apparently due to a more marked vasoconstriction in the skin of the lower extremities than in the upper; however, the cutaneous response may not represent the response in the muscle bed. Fig. 1 serves to present schematically the two divergent mechanisms in the upper and lower extremities.

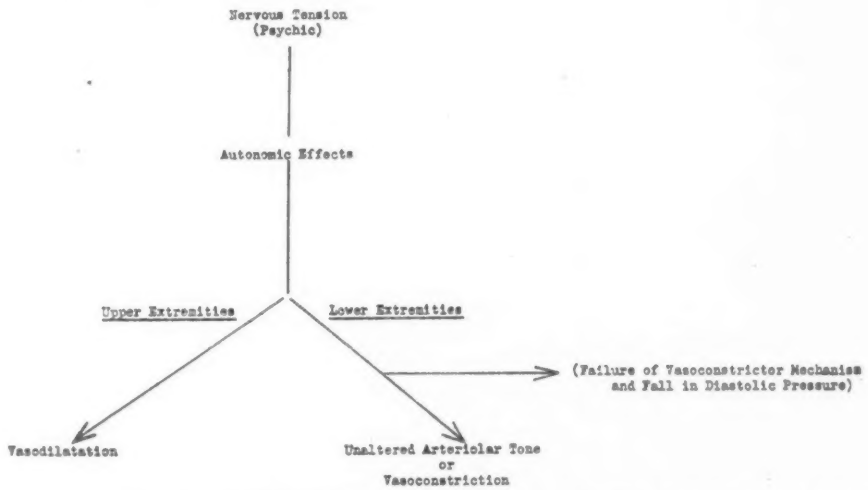

Fig. 1.—Diagram representing the two divergent effects in the upper and lower extremities, and, parenthetically, the potential failure of the vasoconstrictor mechanism in the lower extremities, resulting from a common psychogenic stimulus.

That these cases do not represent functional aortic insufficiency[5,b, 28-30] is evident from the following: (1) An aortic diastolic murmur was absent despite careful, repeated search in a quiet room. Garvin[30] observed aortic diastolic murmurs in all of fourteen autopsied cases of functional aortic insufficiency. (2) A brachial diastolic pressure of "0" is generally not encountered in functional aortic insufficiency. None of Garvin's cases exhibited a "0" diastolic pressure; the diastolic pressure was below 60 mm. Hg in only one of his cases (50 mm. Hg) (3) No evidence, clinical or roentgenologic, of left ventricular dilatation[5, b] was found. (4) The diastolic pressure in the lower extremities did not reveal a corresponding change.

It is to be noted that in many instances neither the brachial systolic nor the popliteal blood pressures exhibited a complete return to normal levels on the return of the brachial diastolic pressure to readings of 60 mm. Hg or above. It is probable that this is due to the fact that the nervous influences were so pronounced that sufficiently basic levels were not attained by our relatively short rest periods. Our rest periods were directed only toward obtaining normal brachial diastolic levels. This further appears to substantiate the view that the syndrome, with its striking feature, a brachial diastolic pressure of "0," represents a marked degree of psychoneurogenic effect on the cardiovascular system. It seems possible, assuming the validity of the second hypothesis, that this same mechanism may extend to so extreme a point where the compensatory vasoconstrictor mechanisms in the lower extremities fail and a temporarily inadequate cerebral flow develops, with resultant syncope. Clinically, syncope

reactions in highly nervous examinees were not unusual. It is likely that various intermediate stages may be encountered in which the diastolic pressure in the lower extremities may exhibit subnormal values (Fig. 1).

White[31] informs the writer that he has seen excitable persons who revealed marked peripheral vasodilatation, but he is not familiar with the circulatory responses in the lower extremities. Peripheral vasodilatation of pronounced degree is occasionally observed in hyperthyroidism[32, 33] and hyperthyroid "crises"[5, c]; apparently the lower extremities share in this response.[34]

It is improbable that the diastolic blood pressure recorded as "0" by the indirect method represents a true 0 pressure. However, it probably does represent, in most instances, a low diastolic level. Its clinical implications, particularly in distinguishing this syndrome from true aortic insufficiency are evident.

SUMMARY

1. In the course of the routine examinations of men between the ages of 18 and 45 years of age for induction into the Armed Forces of the United States, a cardiovascular syndrome, hitherto undescribed, was observed in thirty-eight examinees exhibiting a marked degree of nervous tension.

2. In addition to the nervous element the syndrome was characterized by transient "0" diastolic brachial pressure (indirect method), normal or elevated popliteal pressure, and tachycardia.

3. The brachial systolic pressure associated with the "0" diastolic tension ranged from 118 to 250 mm. Hg and averaged 159.1. The popliteal systolic and diastolic pressures in the prone position averaged 202.[illegible] and 101.9 mm. Hg, respectively. (In the standing position, as would be expected, the popliteal pressures were considerably higher.) The heart rate ranged from 90 to 168 and averaged 127.4. Only two examinees revealed a heart rate below 100.

4. Following rest periods varying between 5 and 90 minutes, the diastolic pressure rose to values ranging from 60 to 112 mm. Hg exhibiting an average level of 75.2. The brachial systolic pressure revealed an average fall of 11 mm. Hg from the initial (prerest) levels. The popliteal systolic pressure in the prone posture exhibited an average drop of 12.5 mm. of mercury. The popliteal diastolic pressure showed an average drop of 7.1 mm. of mercury. (The popliteal blood pressure in the standing position exhibited a corresponding reduction.) The postrest heart rate ranged from 76 to 148, and averaged 104.7, representing a fall of 22.7 beats per minute.

5. The possible mechanisms involved in the genesis of the syndrome are discussed.

6. The clinical implications of this syndrome, particularly in distinguishing it from true aortic insufficiency, are evident.

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A NEW FORM OF GENERALIZED ARTERIAL DISEASE IN NEGROES

Report of Two Cases

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THAT Negroes present medical problems differing from those of Caucasians is well known. Striking examples are the racial incidence of sickle-cell anemia, the rare occurrence of typical acute myocardial infarction among Negroes, the paucity of cases of classical pernicious anemia in them, and their immunity to infectious mononucleosis. It is recognized that thromboangiitis obliterans of the Buerger's type is extremely rare among blacks.[1] We are reporting two practically identical cases of generalized vascular disease in male Negroes, the like of which we cannot find recorded in medical literature. Although the cause is unknown, the condition may properly be called a new form of generalized arterial disease, because clinically and pathologically it differs from all presently known vascular diseases. The only remotely similar form is the syndrome due to occlusion of all arteries which results from syphilitic involvement of the transverse arch of the aorta in which pulsations in the lower extremities are preserved. This syndrome has been described most recently by Aggeler, Lucia, and Thompson.[2]

REPORT OF CASES

Case 1.—The patient, W. W., a male Negro, 30 years old, was admitted to Gallinger Municipal Hospital in a stuporous condition on Aug. 4, 1943. At 10:00 A.M. on Aug. 1, 1944, while still in bed and immediately after coitus, he had had a sensation of contraction in the throat followed by generalized convulsions and profuse perspiration. He was taken to a hospital, given fluid intravenously and some pills by mouth, and then allowed to return home. Another seizure of generalized convulsions developed shortly thereafter, and he vomited several times. The next morning (Aug. 2), he felt much better but became dizzy on standing and was taken to another hospital, where treatment was not given, and on the following morning (August 3) the convulsions recurred. On the morning of August 4, the patient had more severe convulsions, preceded by nausea and vomiting and followed by unconsciousness. After recovering consciousness, he noted that his left extremities were paralyzed. For a short time before the onset of unconsciousness, he had noted transient loss of vision. He stated that for three or four days before the onset of his illness he had been drinking whisky in large amounts, and he attributed his illness to the use of alcohol.

In childhood, the patient had had whooping cough and measles. In 1934 he was in an automobile accident and suffered bruises on both lower extremities and the right side of his face from the eyebrow to the chin. He was unconscious for a short time after that accident but had no disability thereafter. In 1930 he had a urethral discharge, attributed to gonorrhea, which lasted only three days and responded to treatment with "Golden Seal." In 1932 he had a penile sore and received medication intravenously and intramuscularly for a period of one year, after which he was discharged as being cured of the infection, which is thought to have been syphilis. He had been a moderately severe stutterer since childhood and was right-handed. He believed that he had been somewhat "nervous" most of his life and that this symptom had increased in severity during the several weeks prior to the onset of the present illness. For about one year he had noticed that, after a day of unusually prolonged walking, he had developed slight cramps in the left popliteal region, which disappeared shortly if he continued walking. He had no symptoms referable to other systems.

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For many years the patient had been engaged as a truck driver for a transfer company. During the past four or five years he had used about one-half pint of whisky daily but had never developed any illness which was attributed to alcohol. He had been a smoker for fifteen years, and during the past ten years he had averaged about one package of cigarettes daily. No relevant facts were elicited regarding members of his family.

The patient was a well-developed and fairly well-nourished, Negro male who lay quietly in bed without complaints. He was apparently in no distress except for mild apprehension regarding the paralysis. The temperature was 98° F., and the respiratory rate was 20 per minute. The pulse could not be palpated in any of the superficial vessels. Left hemiplegia was immediately obvious. There was very profuse perspiration on the left side of the body, whereas the skin on the right side of the body was unusually dry. The line of demarcation between moist and dry areas was quite sharp in the midline. The pupils reacted normally to light and accommodation. There was a slight or questionable degree of exophthalmos. Ophthalmoscopic examination revealed questionable papilledema; there were no hemorrhages, exudates or other abnormalities. The teeth were extensively carious. The thyroid gland was palpable and seemed to be diffusely enlarged to a slight degree. The lungs were apparently normal. Over the precordium, excessive cardiac activity was visible and palpable. The apical rate was 130 per minute. The cardiac rhythm was regular. The apex beat and left border of cardiac dullness were in the midclavicular line in the fifth intercostal space. No murmurs were audible. The aortic second sound was accentuated. All four extremities were quite cold, more so on the left than on the right. There were no palpable pulsations in the arteries of the arms, legs, or head; slight pulsations were found in the suprasternal notch, the abdominal aorta, and the external iliac arteries. Efforts to measure the blood pressure in each arm were unsuccessful when attempted by members of the resident and visiting staffs. In the lower extremities, the blood pressure was 150/120 over the left popliteal artery and 170/120 over the right popliteal artery. Examination of the neuromuscular system revealed flaccid hemiplegia on the left side with weakness of the left facial muscles. The tongue seemed to deviate to the left side on protrusion. The cremasteric and abdominal reflexes were absent on the left side. Sensation was absent on the left side, as tested by pinprick, stroking with cotton, tuning-fork vibrations, and changes in position.

Laboratory examinations during the course of hospitalization, including urinalysis, hemogram, Kahn test of the blood, blood urea nitrogen, blood cholesterol, and examinations of the spinal fluid were normal or negative. A roentgenogram of the chest was normal. Four electrocardiograms revealed only persistent elevation of the S-T segment in Lead CF_4 of about 3 millimeters. Basal metabolic rates were -15 per cent and -5 per cent. Thorotrast arteriograms of each lower extremity showed filling of the femoral arteries and a few collaterals but not of the tibial arteries. Urologic investigation was negative.

Within a few days the patient's general condition was greatly improved. There was slight fever for only two days. The paralysis rapidly improved and, after several weeks, had almost completely disappeared. Frequent examinations of the peripheral vascular system were made independently by numerous observers. A tabulation of the results of these examinations shows remarkable agreement. The last observation was made on Feb. 24, 1944, after the patient had left the hospital. All examiners stated that there were no pulsations in the arteries of the right side of the head, neck, and the right upper and lower extremities. On only one occasion was the left temporal artery said to be pulsating. The left external maxillary artery was never found to pulsate. The left common carotid was thought to pulsate weakly only on the last examination. The left subclavian and axillary arteries were thought to be pulsating, each on only one occasion. The left brachial artery was thought to pulsate weakly less than half of the time. The left radial was not palpable on most occasions but was well felt on the last. The left ulnar artery was felt to pulsate on the last examination only. The abdominal aorta had strong pulsations throughout. The right external iliac was said to have weak pulsations at first and strong ones later. Pulsation in the right upper femoral artery was felt on a few occasions only and then was said to be weak. The right popliteal artery was felt only once, while the right dorsalis pedis artery was never felt. The right posterior tibial artery in the foot was felt to pulsate from Oct. 19, 1943, on, and was considered to be pulsating normally before the patient left the hospital. The left external iliac artery was pulsating weakly at first, but normally later, whereas the left femoral arterial pulsation, at first imperceptible, later became feebly palpable. The left popliteal artery was thought to be pulsating feebly on one occasion, but the left dorsalis pedis artery was never felt. Pulsations in the left posterior tibial artery were not felt until Oct. 19, 1944, and then appeared, increasing gradually to normal strength.

The blood pressure could not be measured in the right arm until Nov. 4, 1943, and was then recorded at a low level, finally attaining 86/76. In the left arm there was no measurable blood pressure at first, but it became evident at a low level on Sept. 9, 1943, and finally reached 112/98. In the right thigh (popliteal artery) the blood pressure ranged from 158 to 230 systolic and from 90 to 140 diastolic; the last measurement was 190/102. In the left thigh the pressure ranged from 148 to 200 systolic and from 90 to 120 diastolic, the last recording being 180/100. On one occasion 0.03 Gm. of papaverine and, on another, 2 c.c. of Spasmalgin, given hypodermically, did not alter the pulsations or the blood pressure measurements. Oscillometric examinations confirmed these findings.

There were no trophic changes in the extremities; both feet remained equally cool. When last seen, the patient had a very slight residual limp, but other evidences of the paralysis had practically disappeared. His weight had increased from 136 pounds to 151 pounds.

On Aug. 25, 1943, a segment of the right radial artery was removed for histologic examination. There was no bleeding from the artery and only slight bleeding from the veins. Histologic sections of the artery showed a small, star-shaped lumen. There was no evidence of active inflammation (Fig. 1). The intima was not thickened. The media (demonstrated with Mallory's connective tissue stain) had suffered disappearance of most of the muscle fibers with replacement by fibroblasts. Sections stained with Weigert's elastic tissue stain revealed the internal elastic lamina to be somewhat broadened and thickened, with practically no elastic fibers in the media. The adventitia was not altered, and the veins appeared to be normal.

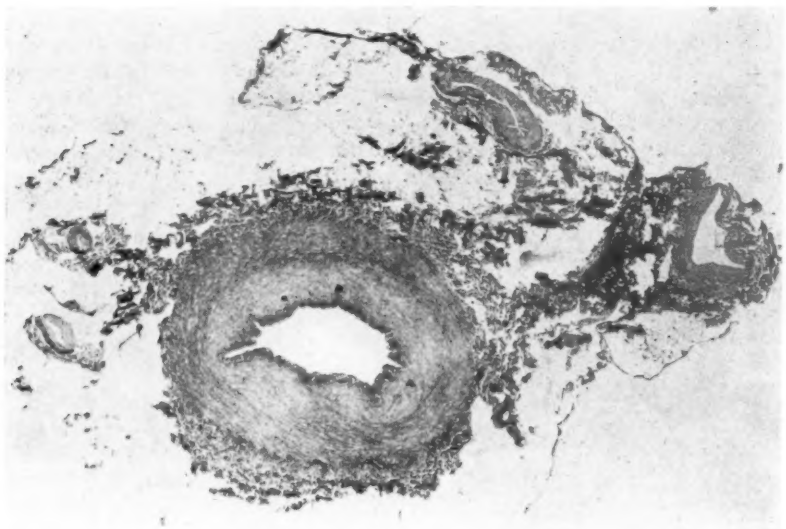

Fig. 1.—Case 1. Cross section of radial artery. Fibrosis of media. Reduced from a magnification of ×30. (Photograph from Army Medical Museum, Washington, D. C.)

CASE 2.—The patient, K. B., a male Negro, 30 years old, was admitted to Gallinger Municipal Hospital at 5:20 P.M. on Dec. 24, 1943. Shortly after awakening at 7:30 A.M., he had developed a severe headache in the right temporal and parietal regions. Within a few minutes he became completely blind in the right eye, and the left upper and lower extremities became paralyzed. Consciousness was lost about 8 A.M., and he was found by members of his family several hours later. During the night before, he had drunk a pint and a half of cheap whisky and had become nauseated, but not intoxicated.

For about a year and a half, the patient had had aching pain in the calves of the legs after walking or running a short distance. Usually the pain began after he had walked one or two blocks and gradually increased, if walking was continued. The pain was more severe in the right calf than in the left. During this time he was employed as a bellboy in a hotel and was able to do his work only because he made short trips. At the same time he had slight impairment of vision in both eyes, but this was not severe enough to prevent his driving an automobile. He had had mild headaches for a long time, and these had been more frequent and more severe during the three weeks prior to the onset of paralysis. There had also been

mild dizzy spells, usually more severe after bending over. In childhood he had had mumps, whooping cough, measles, chicken pox, and scarlet fever. At preschool age there had been an illness of unknown nature followed by slight permanent weakness of the left facial muscles. Pneumonia had occurred in 1940. The patient had had gonorrhea twice, the second time in 1941, but there was no history of syphilis. Tonsillectomy had been performed in 1943 because of frequent sore throat, which did not recur following operation. A pint of whisky had been used daily for a year, about one year before the present illness.

On admission to the hospital the patient was stuporous and somewhat combative when aroused. There was urinary incontinence. He was well developed and well nourished. Complete paralysis of the left side of the body, including the lower half of the face, was obvious, but the deep reflexes were slightly increased on both sides, perhaps a little more on the left. The abdominal reflexes were absent; the cremasteric was absent on the left and present on the right. Babinski's sign was prominently positive on the left and negative on the right. The circumference of the left thigh was 6 cm. less than that of the right. The rectal temperature was 99° F., and the respiratory rate was 20 per minute. Of unusual interest was the absence of pulsations in all peripheral arteries except in the left arm, the femoral arteries in Scarpa's triangle, and possibly the left carotid. There was great tenderness over the right carotid artery, which persisted for at least six weeks. The pulse rate was 80 per minute in the left arm; the blood pressure measured 140/100. Ophthalmoscopic examination revealed pallor of the right optic disc and severe narrowing of the arterioles; the left fundus appeared to be normal. Laboratory tests, including urinalysis, blood counts, blood Kahn test, blood urea nitrogen, blood cholesterol, basal metabolic rate, and examination of the spinal fluid were all normal or negative. Electrocardiograms made on January 21 and February 10 revealed only that the P-R interval was 0.2 to 0.22 second. Urologic investigation was negative.

The status of the patient did not change much during the first week. In the second week the sensorium cleared progressively. During these two weeks the rectal temperature ranged daily between 100° F. and 101° F. By the fourth week the patient was able to stand, and by the sixth week he was able to use his arm and leg to about 50 per cent of normal capacity. At this writing, Oct. 28, 1944, there is still a limp, some clumsiness of the left hand, and almost complete paralysis of the lower half of the left side of the face. There is complete right optic atrophy. The reflexes are normal.

During these ten months of observation, the peripheral vascular system was examined repeatedly by numerous physicians. A tabulation of these examinations reveals that the right temporal artery was found to be pulseless except on two or three occasions when it was thought to have a faint pulsation; the right carotid artery was always pulseless, as was the right external maxillary; the right subclavian artery was pulseless except during the last two months; the right axillary artery was pulseless until now, the time of writing, when it appeared to pulsate normally; and the right brachial, radial, and ulnar arteries were continuously pulseless. Pulsations of the right femoral artery were recorded as varying from absent to normal, but were usually present; but the right popliteal, dorsalis pedis, and posterior tibial arteries were always pulseless. On the left side the temporal artery was usually recorded as pulseless, the carotid pulsation as absent or weak, the external maxillary as absent or weak, the subclavian from absent to normal, and the axillary, brachial, radial, and ulnar pulsations were usually normal, although recently weaker. The pulsations of the left femoral artery were recorded as being absent, weak, palpable, normal, or strong, but definitely present; the left popliteal artery was recorded to have pulsations ranging from absent to strong but recently weak, and the same statement applies to pulsations of the left dorsalis pedis and posterior tibial arteries, which are now very weak. Oscillometric examinations corresponded with these results.

Blood pressure measurements were obtainable only in the left arm and the left thigh. In the former, they were usually about 130/90; whereas in the left thigh (popliteal region) they were not obtainable until April, since when they have varied from 150 to 215, systolic, and 100 to 160, diastolic. On the last examination the reading was 155/100. On April 13, 1944, following the intravenous injection of 60 mg. of papaverine, there was no appreciable change in the degree of any arterial pulsation or in the blood pressure readings.

There have been no trophic changes of the extremities or digits. The feet have been relatively cold. At first, the right was cooler than the left, but recently the left foot has become considerably cooler than the right.

On Jan. 11, 1944, an arteriogram of the right leg, obtained by injecting Thorotrast into the right femoral artery in Scarpa's triangle, failed to show filling of the arteries below the middle of the thigh. On April 4, 1944, a left carotid arteriogram, made by injecting the Thorotrast directly into the common carotid artery through the skin, showed filling of all

cerebral vessels of the left hemisphere but none of the right. This test was repeated on Oct. 11, 1944, after surgical exposure of the artery, and revealed the same condition. On direct examination during operation the artery appeared to be much thicker than normal.

On Jan. 1, 1944, a biopsy was made of the left posterior tibial artery. Both vein and artery were of small diameter. The vein was patent, but the lumen of the artery was very small; both were bloodless. On Oct. 18, 1944, Dr. J. Ross Veal exposed the right common carotid artery and found it pulseless and solid. The veins were patent, and there were no adhesions around the vessels. A segment of the artery was excised without the need for ligation. Sections of the posterior tibial artery showed the vessel to be thickened and the lumen slitlike (Fig. 2). The intima was slightly thickened. The media was interspersed with fibrous tissue which had replaced about 60 per cent of the muscle fibers. The internal elastic lamina was moderately thickened. The adventitia appeared to be normal. There were no active inflammatory elements. The veins were apparently unaffected.

Examination of sections of the right carotid artery show the lumen to be eccentric and reduced to about one-third normal size and filled with an unorganized clot (Fig. 3). The remainder of the old lumen was filled with organized tissue which may have been the result of subintimal proliferation. All of the blood vessels in this tissue were small endothelium-

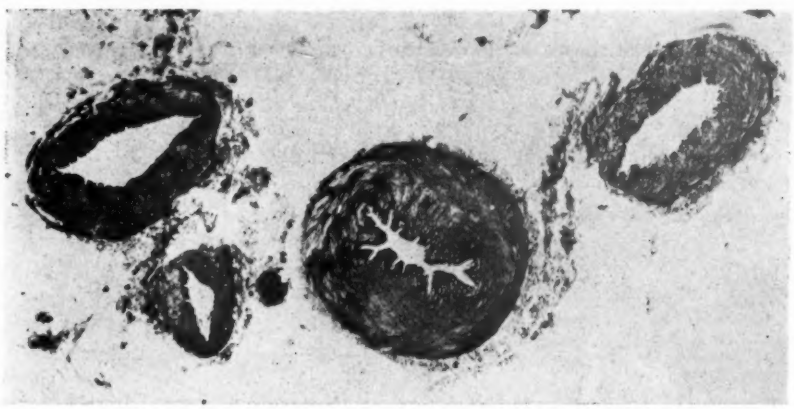

Fig. 2.—Case 2. Cross section of dorsalis pedis artery with vena comitantes. Slitlike lumen with severe fibrosis of media of artery. Reduced from a magnification of ×30. (Photograph from Army Medical Museum, Washington, D. C.)

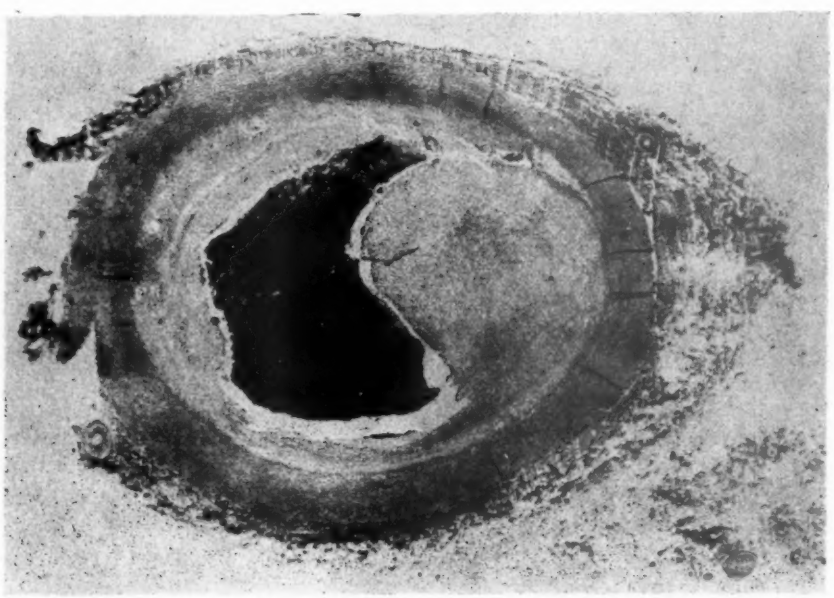

Fig. 3.—Case 2. Cross section of right common carotid artery. Subintimal proliferation with reduction of size of lumen, which is filled with unorganized clot. Reduced from a magnification of ×15. (Photograph from Army Medical Museum, Washington, D. C.)

lined spaces. This tissue looked like a network with irregularly sized, rounded spaces interspersed with darkly staining nuclei. Some of the spaces appeared to have contained cholesterol, but a stain for fat was not made before embedding. The presence of mucin was ruled out by means of a mucicarmine stain. The spaces were probably, therefore, the result of edema. The media had been replaced largely by connective tissue, most notably in the inner half (Fig. 4), as shown by Brilmeyer's stain. Sections stained with Weigert's elastic tissue stain showed a moderately disrupted internal elastic lamina, and the elastic fibers of the media seemed to be denser than normal, but this effect might be due to narrowing of the

Fig. 4.—Case 2. Fibrosis of media and subintimal proliferation of right common carotid artery; small artery in adventitia on left, with small lumen and subintimal proliferation. Reduced from a magnification of ×100. (Photograph from Army Medical Museum, Washington, D. C.)

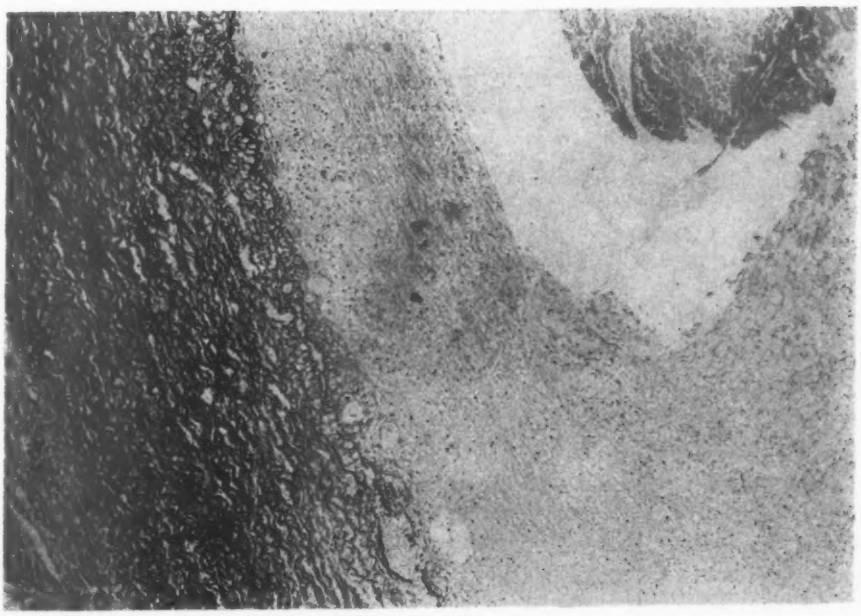

Fig. 5.—Case 2. Elastic tissue stain of right common carotid artery; media and subintimal proliferation shown. Reduced from a magnification of ×100. (Photograph from Army Medical Museum, Washington, D. C.)

media from contracture (Fig. 5). The small arteries in the adventitia had small lumens and greatly thickened walls due to marked subintimal proliferation, and there was great reduction in the thickness of the media. Nowhere was there any evidence of inflammation.

DISCUSSION

The only vascular disease of known cause is that due to syphilis. So far as our definite knowledge is concerned, the only vessels of the body affected by syphilis are the aorta and other large arteries and the small arteries of the central nervous system. Cases of disease of the medium-sized arteries, particularly of the extremities, have been reported as being caused by syphilis, but the proof is inadequate. Because syphilis is so prevalent among Negroes, it is not unnatural to try to attribute arterial disease in members of this race to this cause, when a definite etiological diagnosis cannot be made. Although one of our two patients had had syphilis, there is no histologic or other evidence that the vascular disease is of that origin. Neither patient had evidence of aortitis or of syphilitic disease of the central nervous system, and Kahn tests on both were negative.

In 1937, one of us (W. M. Y.)[1] reported five cases of thromboangiitis obliterans in male Negroes. The lower extremities were mainly affected. On the whole, the findings in these cases closely resembled those of Buerger's disease in Caucasians. One of us (W. M. Y.) has not observed any more cases of vascular disease resembling Buerger's disease among Negroes, but an additional patient with this condition has been treated in this institution by Dr. J. Ross Veal. Two of the five patients reported have remained under observation. One (Case 1) has not had any further symptoms referable to his feet, which he has excellently cared for. He is now suffering from chronic congestive heart failure, the result of calcific aortic stenosis and regurgitation. The other patient (Case 4) has had no further symptoms except for an attack of acute superficial phlebitis which responded promptly to treatment. All five of the patients had or had had syphilis, but biopsies of their arteries did not reveal evidence of that disease.

These two new cases of unusual vascular disease in male Negroes cannot be explained, but it is our opinion that there have been multiple silent episodes of thrombosis in medium-sized, and even larger, arteries, mainly of the peripheral vascular tree. The first symptom was the onset of intermittent claudication and this was followed, more dramatically, by thrombosis in an artery serving the brain. That this thrombosis might have been the result of acute arteritis was suggested by the extreme tenderness over the right carotid artery in Case 2, but histologic examination of the artery ten months later did not reveal any residual inflammation, which might have been expected to persist. It was baffling and astounding to all observers to see two patients without pulsations in practically all of the peripheral arteries, a phenomenon which none had previously seen in living subjects not in a state of extreme shock.

The study of the biopsy specimens in the two cases did not help to elucidate the nature of the disease. That the arteries were occluded proximal to the area of biopsy was shown by the lack of bleeding when the sections of the arteries were excised. The fibrosis of the media and the small size of the lumen could have been the result of disuse alone. That the lack of pulsations in so many arteries was not due to spasm was demonstrated by the fact that antispasmodics did not produce any change and that, as the months passed, there was very moderate improvement in the amplitude of pulsations. The collateral circulation was adequate, as attested by the absence of trophic changes, except following the cerebral episodes which left slight residual defects.

In the sections of arteries examined there was no evidence of active inflammation. The fibrosis was confined to the media, and there was no indication of previous periarterial inflammation. The carotid artery in Case 2, examined by biopsy ten months after the development of the hemiplegia, showed irregular and extreme subendothelial proliferation and some disruption of the internal elastic lamina. Strangely, the clot in the narrowed and irregular lumen showed no organization. The small arteries surrounding the carotid also showed subintimal proliferation and reduction in size of the lumen.

The absence of inflammatory elements in the biopsy specimens leads us to suggest the possibility of some chronic intoxication that lead to degenerative changes of the intima at certain points, with resultant subintimal proliferation and, eventually, thrombosis. That "essential thrombophilia," as described by Nygaard and Brown,[3] was not the cause of the thromboses is shown by the absence of venous thromboses. The disturbance in our two patients is distinctly arterial.

The findings in the two cases showed no similarity to periarteritis nodosa.[4, 5] They are certainly not similar to those of generalized thromboangiitis obliterans of the Buerger's type, either clinically or histologically. The cerebral vascular accidents were undoubtedly the result of thrombosis of the common carotid artery (Case 2) and of either the common carotid or the internal carotid arteries (Case 1). In cases reported as cerebral thromboangiitis obliterans, cerebral vascular phenomena have apparently been the result of widespread involvement of the small vessels in the brain,[6] rather than in the larger arteries, and inflammatory elements have been present.

SUMMARY

Two cases of a previously undescribed form of arterial disease have been reported. Both patients were male Negroes, 30 years of age, who were well except for recent intermittent claudication, until affected by hemiplegia of sudden onset. Pulsations were absent in practically all of the peripheral arteries except the upper femorals, and in greatly reduced intensity in a few others. A striking feature was the absence, or great impairment, of pulsation in the arteries of the neck and head. The nature of the disease could not be ascertained. It is postulated that an arterial degeneration of unknown cause resulted in multiple thrombotic episodes in numerous portions of the peripheral vascular tree, including those of the head and neck.

The photomicrographs used herewith were made by Mr. Roy M. Reeve, Army Medical Museum, Washington, D. C., negatives numbered 83944 through 83948.

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THE EVALUATION OF VASCULAR RESERVE IN PERIPHERAL VASCULAR DISEASE

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ALTHOUGH clinicians in the past were well acquainted with the symptoms and signs of peripheral vascular disease, it was not until the last two decades that methods were described to test the patency of the blood vessels of extremities. In 1926, Brown[1] obtained vasodilatation by means of intravenous administration of typhoid vaccine. In May, 1930, White[2] and Brill and Lawrence,[3] at the same time, but working independently, showed that spinal anesthesia caused an increase in the surface temperature of the feet. Scott and Morton,[4] in June, 1930, found that general anesthesia gave the same complete abolition of vasoconstriction. Again, in October, 1931, Scott and Morton[5] injected the posterior tibial nerve to differentiate arterial spasm from organic obstruction. Sir Thomas Lewis,[6] in 1929, used heat to induce peripheral vasodilatation, and, in 1932, Gibbon and Landis[7] produced a similar reflex result in the legs by immersion of the forearms in warm water. The latter authors decided, in 1933,[8] that the immersion test compared favorably with the other methods of vasodilatation. In 1938, Beck and deTakats[9] injected sodium nitrite intravenously and observed the increase in oscillations, as measured by the oscillometer.

When one who works with peripheral vascular disease is presented with such a variety of procedures, he is really at a loss to know which method he should use, from the point of view of ease of procedure and dependability of result. It is not very feasible, of course, to give a patient spinal or general anesthesia for the testing of vasodilatation, especially as a clinic or office procedure. For the past eight years, therefore, we have experimented with the various methods of producing vasodilatation, and the details of these findings may be found in other publications.[10, 11] The final conclusion from all these studies was that novocain block of the common peroneal and posterior tibial nerves was the test of last appeal to determine whether full vasodilatation could be obtained, and the measure of the degree of vasodilatation was designated as vascular reserve.

Due to the fact that many who work with peripheral vascular disease block only the posterior tibial nerve and omit the common peroneal, it was felt that we should determine to our satisfaction whether or not that procedure alone was sufficient to give full vasodilatation. We desired to find out if it was necessary to include the common peroneal or if blocking the common peroneal was a superfluous procedure.

PROCEDURE

We chose twenty patients in whom full vasodilatation had been obtained by blocking both the common peroneal and posterior tibial nerves with 2 per cent novocain without adrenalin. The diagnoses in these cases were as follows: arteriosclerosis obliterans, eight; no peripheral vascular disease, six; postphlebitic syndrome, two; vasospasm, two; scleroderma, one; thromboangiitis obliterans, one.

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After full vasodilatation had been shown, block was produced in each patient at two subsequent visits to the clinic; at one time the posterior tibial nerve alone was blocked, and on the other visit the common peroneal nerve was injected. No readings were considered valid unless the nerve block had been definitely confirmed as follows: Block of the common peroneal nerve was indicated by (1) loss or diminution of sensation of the entire dorsum of the foot, or (2) inability to flex dorsally the toes of the foot, inability to flex dorsally the foot on the ankle, and inability to evert or invert the foot. Block of the posterior tibial nerve was demonstrated by loss or diminution of sensation on the plantar aspect of the foot. The common peroneal nerve was blocked at the neck of the fibula, and the posterior tibial nerve was blocked 1 inch above the lower end of the internal malleolus on the posterior aspect.

All tests were carried out with the room temperature below 26° C.; it was often as low as 19° C. and once went as low as 16.1° C. Block was not attempted unless the temperature of the large toe, to be tested, was below 26° C. Often the toe temperature was nearer 20° C. Full vasodilatation was indicated by a temperature of at least 30° C. one hour after confirmation of the block. All readings were made at the base of the nail of the large toe, and were taken with the Taylor dermatherm. The results were estimated in percentage rise from the starting temperature below 26° C., to 30° C. For instance, if the temperature on the large toe before the block was 20° C., a rise to 30° C. represented 100 per cent vasodilatation; likewise, a rise at the end of one hour to only 28° C. represented eight-tenths or 80 per cent vasodilatation. Only one case was included that showed a rise to only 29.5° C. after blocking both nerves.

RESULTS

Blocking of both the common peroneal and posterior tibial nerves. All patients showed a rise from below 26° C. to at least 30° C., except the one mentioned above which showed a rise to only 29.5° C.

Block of the posterior tibial nerve only. Eleven of the twenty patients showed a rise to 100 per cent; one showed no rise at all; and the other eight showed increases of 56, 60, 75, 80, 80, 85, 87 and 91 per cent, respectively.

Block of the common peroneal nerve only. The data in three cases were not recorded; three patients showed no rise at all; and the others showed increases of 8, 23, 27, 27, 33, 40, 50, 59, 63, 71, 80, 82, 86, and 100 per cent, respectively.

COMMENTS

In May, 1940, we published criteria for the classification and diagnosis of peripheral vascular diseases.[12] At that time we emphasized the point, that it was important in reporting results of therapy, that the initial status of the patient be determined, that some method be established to determine progress, and that uniform diagnostic standards be established to make possible valid comparisons of data from many sources and to permit crystallization of prognostic and therapeutic principles from these data.

We also felt, as we do now, that determination of vascular reserve is the most important single objective in the study of the patient. It is a measure of degree of vascular impairment and an indication of how much we may hope to attain with suitable therapy. Periodic determination of vascular reserve is useful also as a means of following changes in the vascular status of the patients' limbs. The only known way to determine this vascular reserve is by vasodilatation tests,

and the only methods that give the answer unequivocally are those that eliminate the vasoconstrictor pathways. These methods in the past have proved to be paravertebral block, sympathectomy, spinal or general anesthesia, and peripheral nerve block; and, as has been shown in this communication, in the case of peripheral nerve block, one must employ block of both the common peroneal and the posterior tibial nerves simultaneously.

CONCLUSION

Twenty patients, in whom novocain block of the common peroneal and posterior tibial nerves produced complete vasodilatation, were tested subsequently by blocking the common peroneal and posterior tibial nerves individually at different times. It has been shown that, while block of the posterior tibial nerve alone gives more efficient vasodilatation than block of the common peroneal alone, one must block both nerves simultaneously in order to get a dependable and unequivocal result. Block of either one of these nerves alone cannot be relied on to give the maximum vasodilatation at all times.

We wish to give credit to Mrs. Rosa Abraham, R.N., and Mrs. Leah Banks for their valuable technical assistance.

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Clinical Reports

ELECTROCARDIOGRAMS SIMULATING POSTERIOR MYOCARDIAL INFARCTION AFTER CESSATION OF PAROXYSMAL TACHYCARDIA

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THE purpose of this paper is to report another cause for abnormal S-T and T changes other than myocardial infarction. Geiger[1] reported such a case in a recent issue of THE AMERICAN HEART JOURNAL. I wish to add this case to the literature.

CASE REPORT

O. C., a 62-year-old farmer, registered in the Clinic on Nov. 3, 1942. His chief complaint was "heart attacks." These consisted of an exceedingly rapid heart rate associated with nausea and vomiting. His heart attacks began five years previously. At that time he would go for many months without having an attack, but later they were more frequent. Some of the attacks lasted only a minute, but some continued as long as eight hours. The onset and cessation of the attacks were instantaneous. Previous to his last attack, he would be able to resume his duties as soon as his heart returned to a normal rate. His last attack occurred six days prior to registration. With most of these seizures he would have a choking sensation and pain in the neck. With the most severe attacks he would suffer nausea and vomiting. The last attack also was associated with severe epigastric pain. This had disabled him so that he felt weak, lightheaded, and staggery. It was the patient's thought that certain foods, such as apples and other fruits, might bring on an attack. He had to take a laxative twice a week. His systemic history was otherwise negative except for rheumatism that had existed for twenty-five years. His family history was negative except that his father died at 80 with gangrene of the foot. His marital history was negative.

Physical examination revealed a man 66 inches tall and 121½ pounds in weight. The blood pressure was 145/88 in both arms; the pulse was 58; and the temperature was 97.6° F. His teeth were deserving of x-ray study. The nasal mucosa was of the chronic catarrhal type. The tonsils were normal. The heart and lungs were normal physically. There was tenderness over the spine, left costovertebral area, and right costal margin.

Because paroxysmal auricular tachycardia and rheumatism may be associated with foci of infection, numerous laboratory studies were done. Complete blood counts, blood Mazzini, and blood sugar were normal. The blood uric acid was 4.1 milligrams. The urinalysis, gastric analysis, and basal metabolic rate were normal. Although his prostatic secretion revealed no pus cells, the dextrose brain broth culture produced a streptococcus. The stool culture was negative. The electrocardiogram was normal (Fig. 1). The chest film revealed a normal cardiac silhouette and normal lung fields. Intravenous pyelograms were normal but marked arthritic changes could be seen in both hip joints and lumbar spine. Cystoscopic examination was negative except for slight prostatic enlargement and a small stricture in the membranous urethra. A gastrointestinal series and barium enema were normal except for hypertonicity. Cholecystograms were normal. Dental rays revealed periapical infection on number 23 and pyorrhea, Grade 4, on the lower anterior teeth.

Our diagnosis was paroxysmal auricular tachycardia in an otherwise normal heart. He also had an abscessed tooth and pyorrhea with osteoarthritis.

The patient wasn't seen again until the morning of Nov. 25, 1942. Two nights previous to admission he suffered another attack of tachycardia. This was associated with pain in the neck and a choking sensation. He was in a state of shock. His lips and fingernails were blue. The radial pulse was imperceptible, but the apex beat was 220. The blood pressure was 50/40. There were râles in both lung bases.

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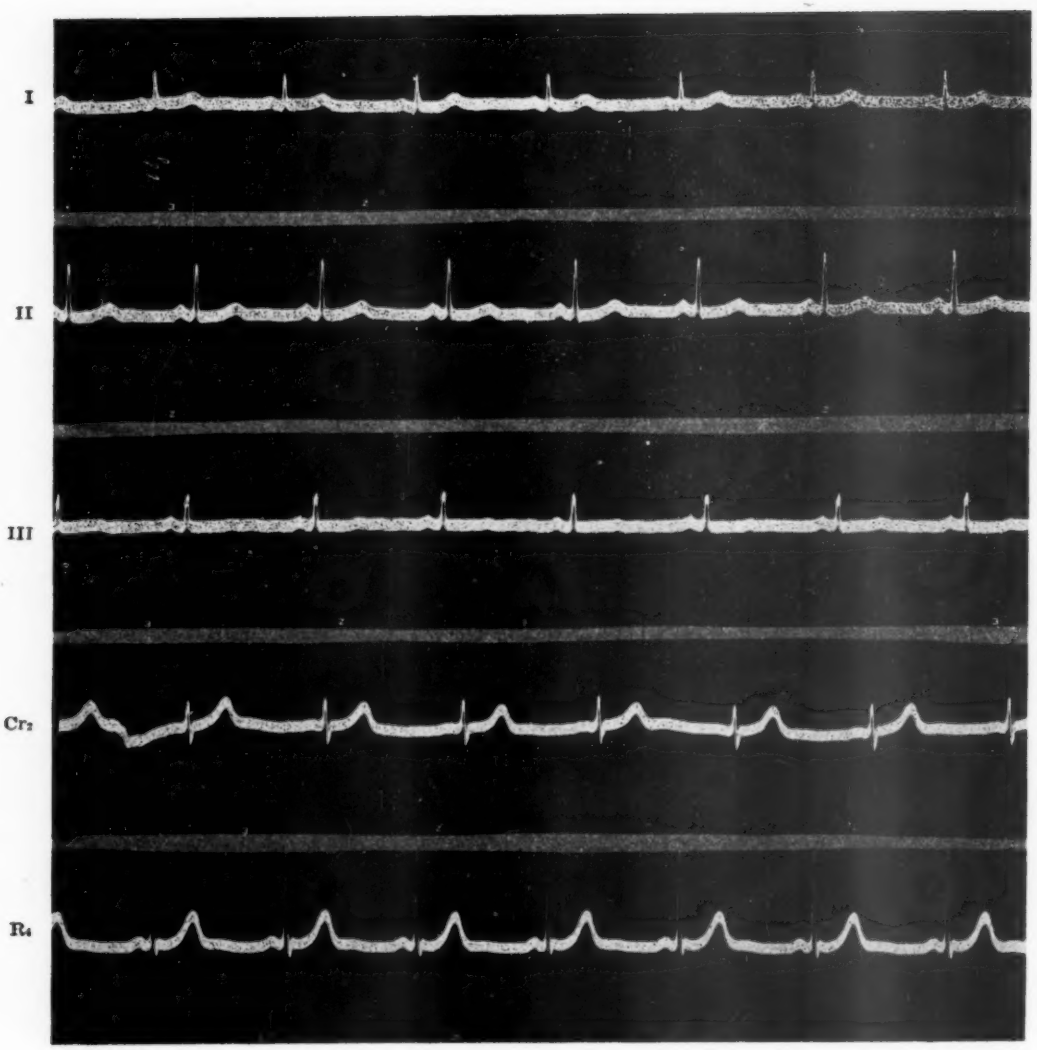

Fig. 1.—Electrocardiogram taken when patient was first seen on Nov. 11, 1942.

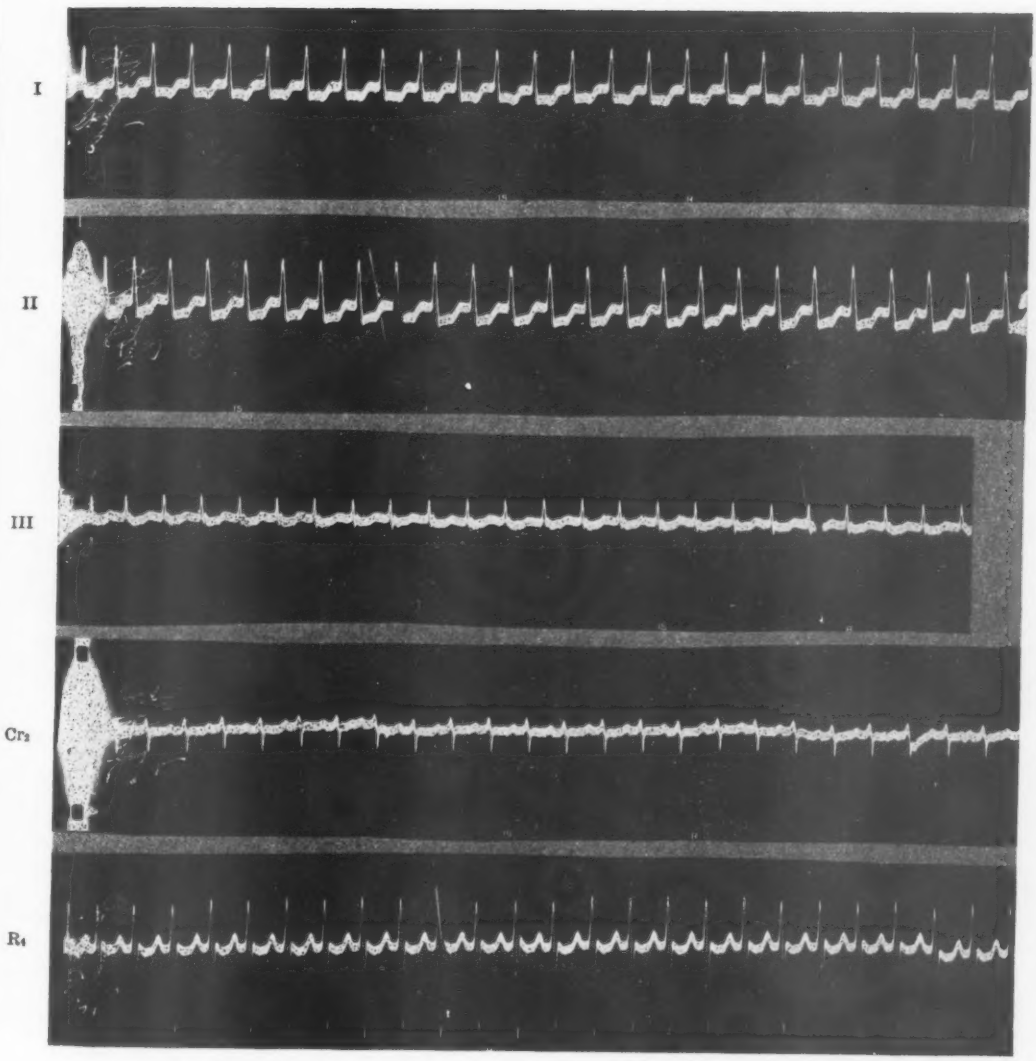

Fig. 2A.—Electrocardiogram taken when patient returned on Nov. 25, 1942, sixty hours after onset of an attack of paroxysmal auricular tachycardia. Note S-T depression and effects on T waves.

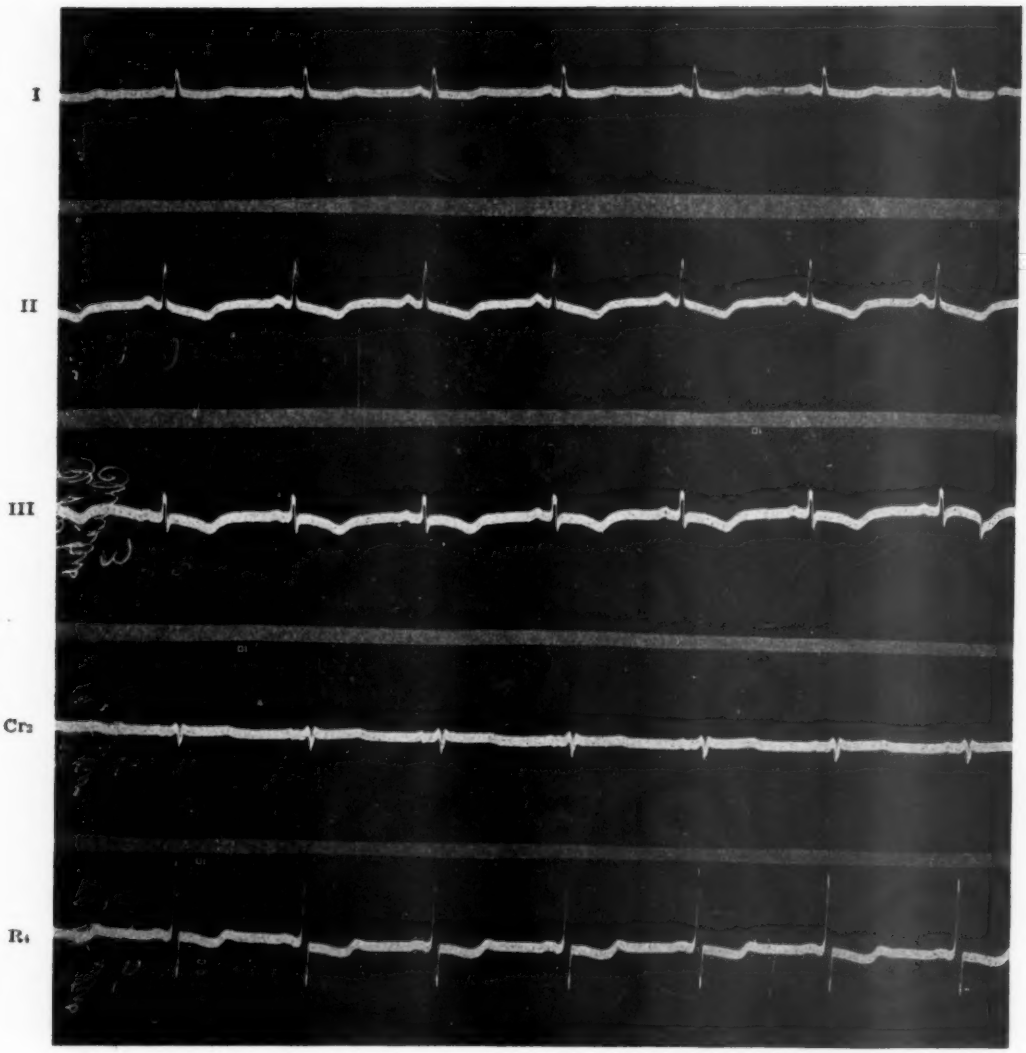

Fig. 2*B*.—Electrocardiogram taken on Nov. 28, 1942, showed T changes suggesting myocardial infarction.

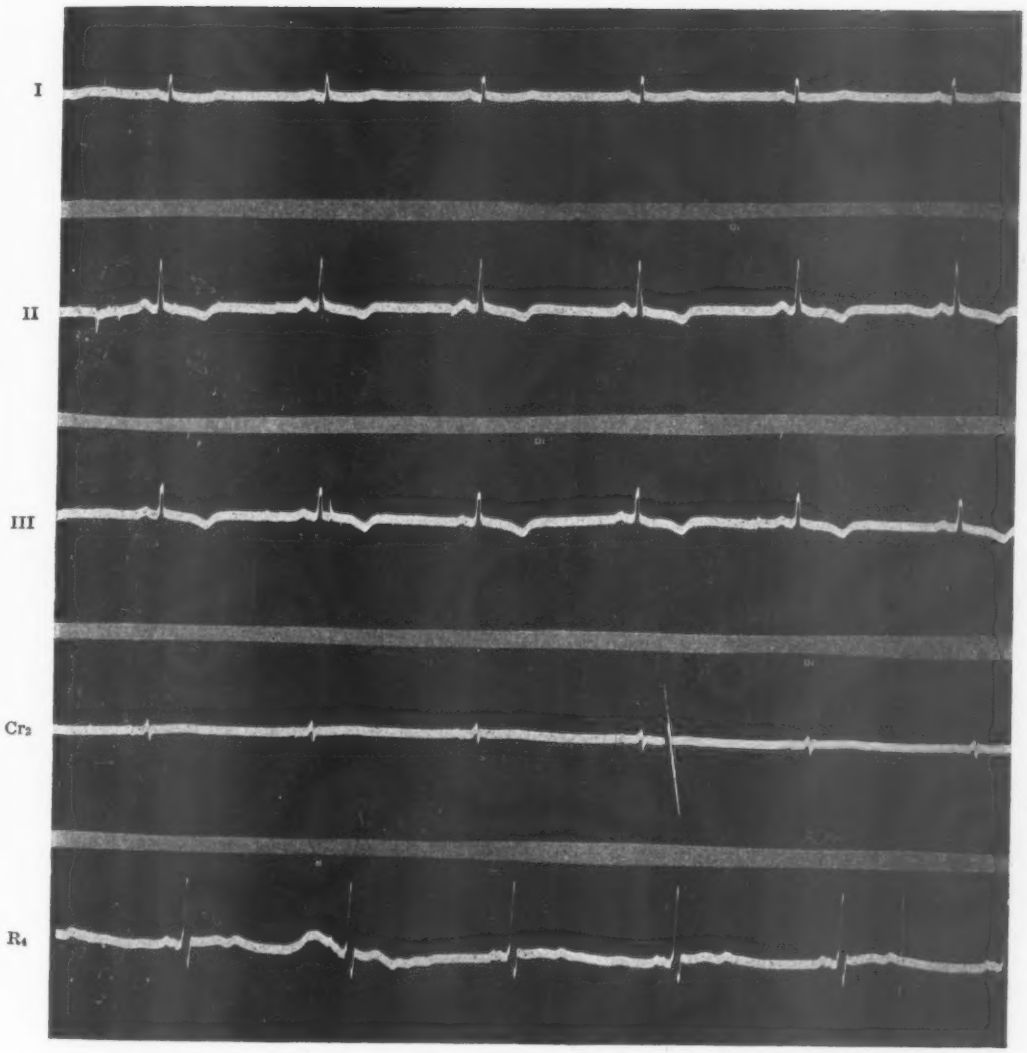

Fig. 2*C*.—Electrocardiogram taken on Dec. 4, 1942. By now the digitalis effect was worn off and T_1 is upright but $T_{2,3}$ and CR_4 are still inverted.

The electrocardiogram showed a rate of 220 with S-T depression and corresponding T changes in all leads (Fig. 2*A*). Neither ocular pressure nor carotid sinus pressure helped. At 8:30 P.M. the radial pulse and blood pressure were not obtainable. The apex beat was 220 per minute. However, his color was improved due to the inhalation of 100 per cent oxygen by mask. One hour later since there was no change for the better, 5 c.c. Digiglusin were given intravenously. By 1:30 A.M., Nov. 26, 1942 (four hours later), the radial pulse was regular at 88 beats per minute. By 8:30 A.M., the pulse was 74, the blood pressure was 115/85, and the color was pink. On Nov. 28, 1942, the electrocardiogram showed a rate of 70 with a normal sinus rhythm. T_1 tended to be diphasic but $T_{2 \text{ and } 3}$ were inverted and CR_4 was diphasic. (See Fig. 2 to note progressive improvement and return to normal within two months' time.)

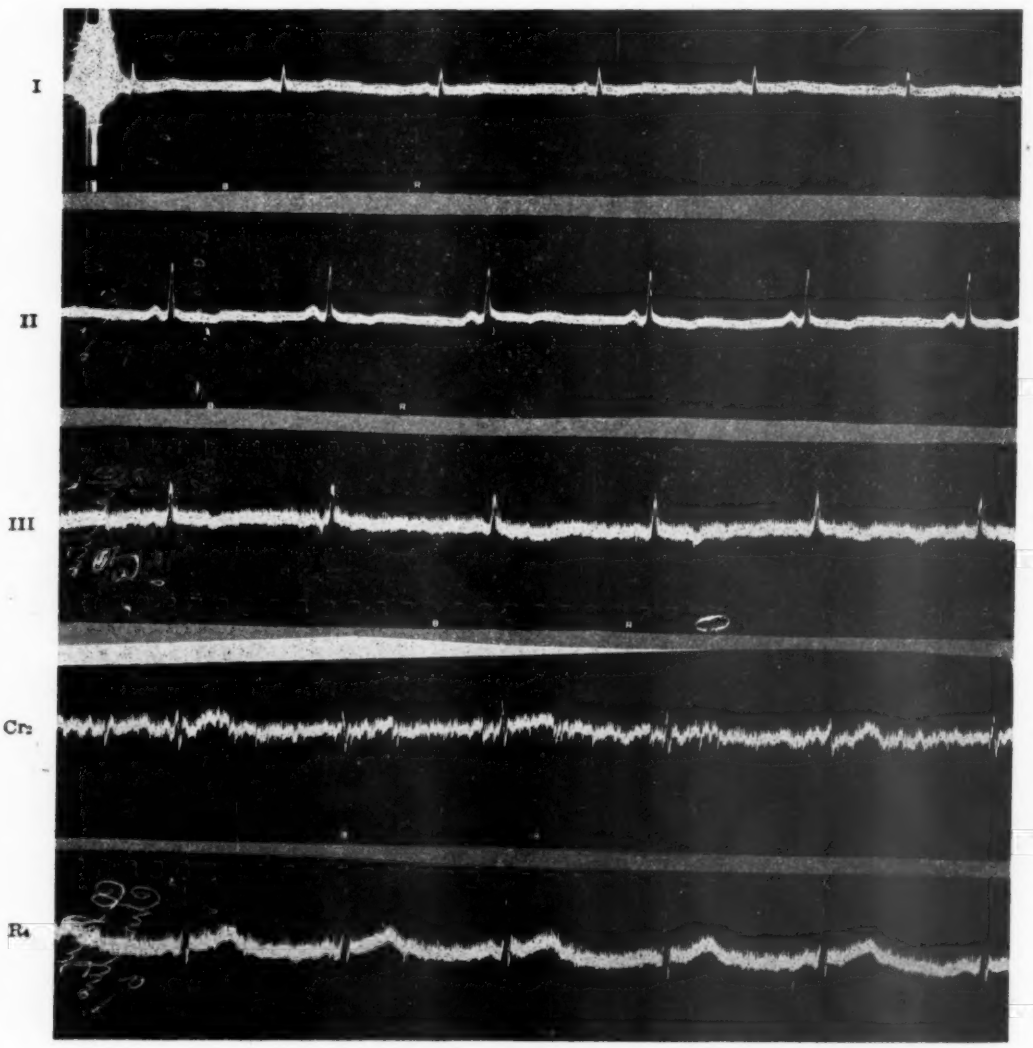

Fig. 2*D*.—On Dec. 10, 1942, $T_{2 \text{ and } 3}$ were inverted but CR_4 was upright.

The patient remained hospitalized until Dec. 18, 1942, because it was thought he had a coronary occlusion. His treatment consisted of continued rest, aminophylline, a nerve sedative, and quinidine. It was hoped that this would prevent another attack.

He returned for examination on Jan. 28, 1943. He had suffered no symptoms from his heart, but his rheumatism was worse. His blood pressure was 170/100, but his electrocardiogram had returned to normal (Fig. 2*F*).

The patient was not seen again until Feb. 10, 1943. He was doing nicely until two nights before admission when a similar type of heart attack was encountered. The patient when first seen again was very pale and cyanotic. He was listless but had an apprehensive

look. The pulse rate was 200, and the blood pressure 75/60. The electrocardiogram (Fig. 3*A*) showed an A-V rate of 200. Notching is present in all QRS complexes. There is depression of the S-T segment with diphasic T waves in all leads.

Five cubic centimeters of digiglusion were given immediately and oxygen was started. Twelve hours later the pulse was still 200, so 3 c.c. more of digiglusin were given intravenously. It was two days later before the pulse returned to a normal level. A total of 10 c.c. of digiglusin were required this time to produce a normal sinus rhythm. (See Fig. 3*B* for the electrocardiographic changes.) This attack was quite shocking to the patient, and it seemed to take several days for him to regain his strength. Within ten days he was feeling quite well, and we permitted him to leave the hospital in two weeks.

We now felt that these T changes were functional in origin as a result of the paroxysmal auricular tachycardia.

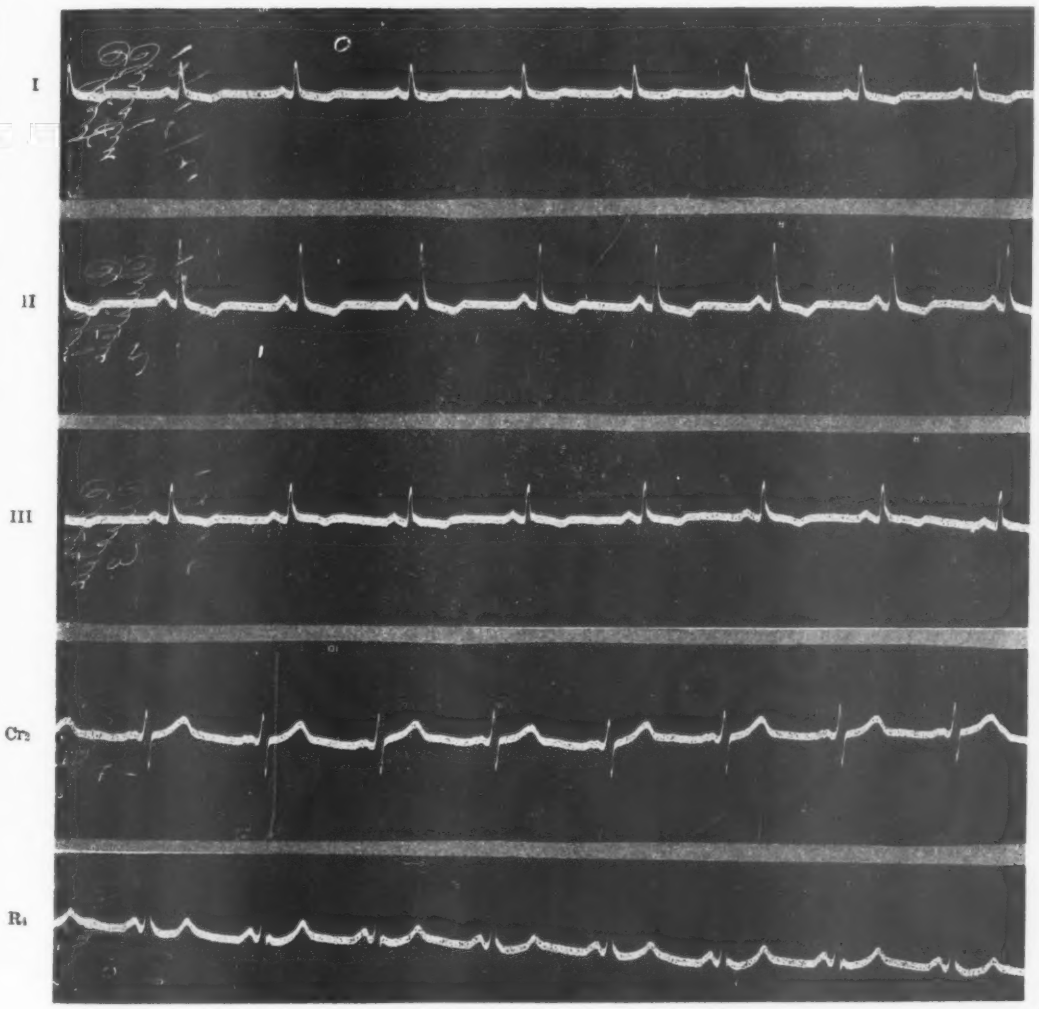

Fig. 2*E*.—On Dec. 18, 1942, the T waves were inverted in all of the standard leads but CR_4 was still upright. Why T_1 is inverted in this tracing is unexplained.

DISCUSSION

As Geiger[1] pointed out, it is very important to differentiate this type of T change due to functional disorder from that due to a coronary occlusion.

The most common age for paroxysmal auricular tachycardia to occur is between 20 and 30 years, but in this case the patient was 62 years, an age at which coronary occlusion commonly occurs. All clinical and laboratory evidence favored a normal heart except those electrocardiographic changes immediately following the attacks. It is of importance to note that the patient was first

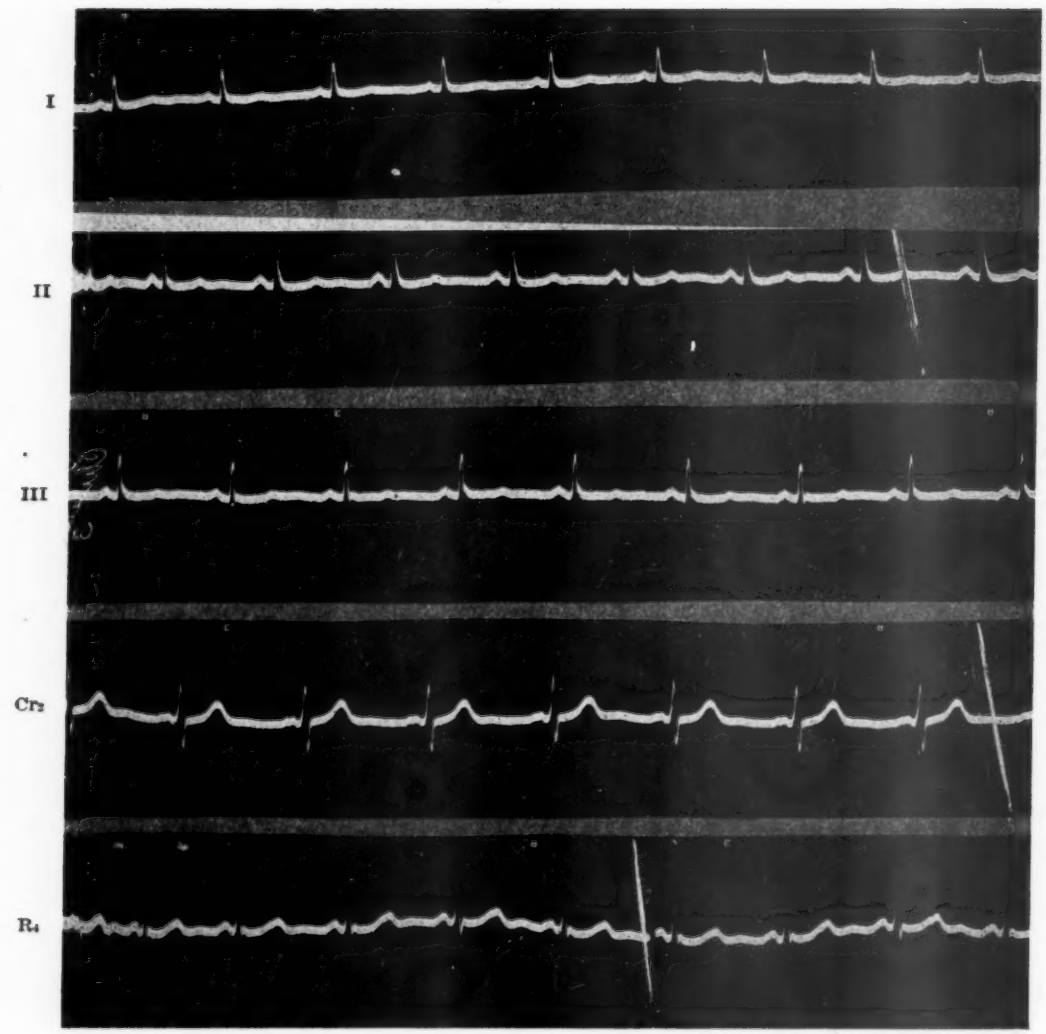

Fig. 2*F*.—On Jan. 28, 1943, the T waves were upright in all leads.

seen six days after an attack and had a normal electrocardiogram, but the next two attacks produced T changes. A recent communication (Feb. 8, 1944) with the patient was encouraging. He had had only three light attacks and had gained in weight and strength.

There are a few changes in these tracings differing from the usual patterns of coronary occlusion. The S-T changes are depression in all leads with T-wave inversion during the stage of tachycardia. Also there are no Q waves. No more than 5 c.c. of digiglusion were required to stop the first attack. No more

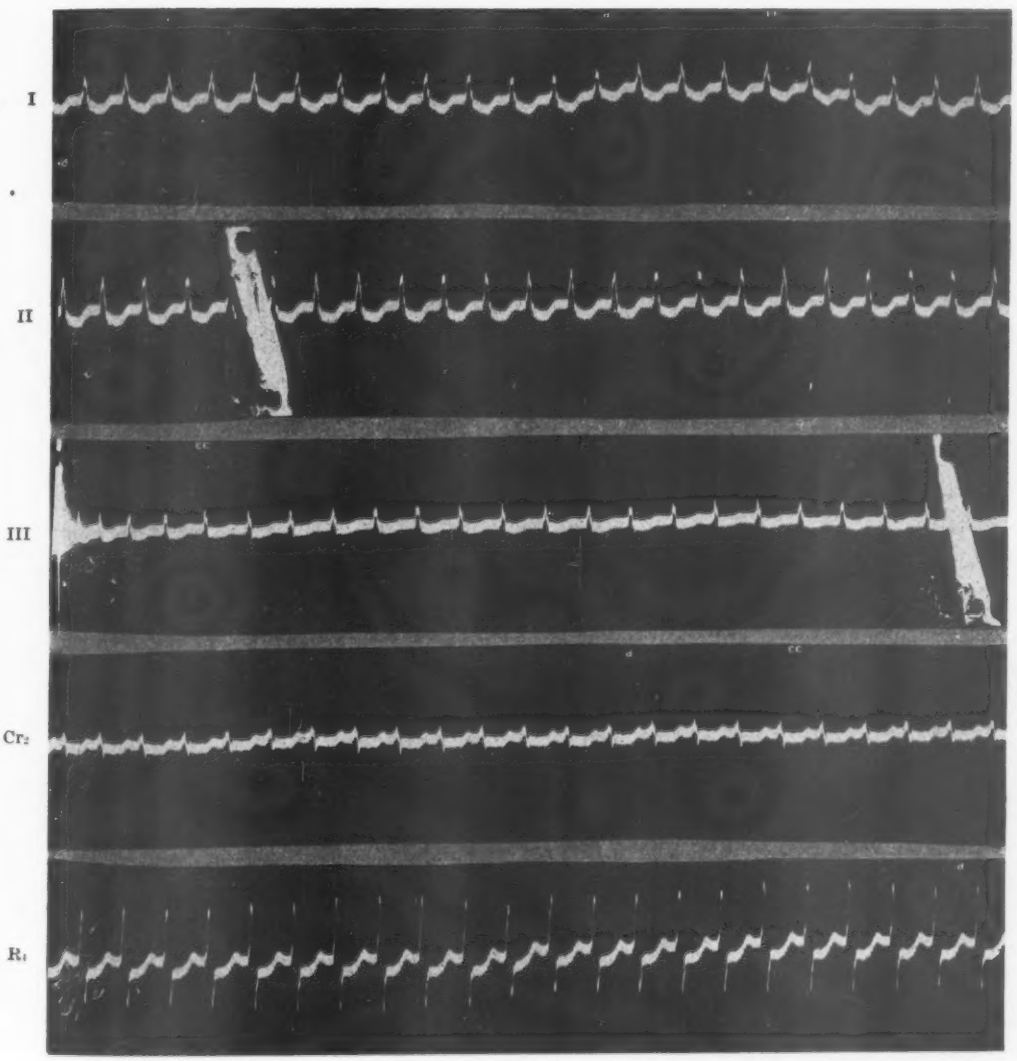

Fig. 3A.—Electrocardiogram taken on Feb. 11, 1943, three days after onset of attack. The rate was 200 per minute. Note notching of QRS complexes, depression of S-T segments in all leads, and T-wave changes.

digitalis was given. Consequently, it was not a digitalis effect that maintained the T changes after cessation of the tachycardia. Seeing this type of patient for the first time shortly after an attack and obtaining this type of tracing certainly puts one on the alert.

We agree with Geiger that the probable cause of these changes is a temporary ischemia to an area of myocardium which heals by resolution rather than scarification. This patient suffered ischemic pain as suggested by distress in the epigastrium and radiation into the neck.

SUMMARY

A case is presented of paroxysmal auricular tachycardia producing electrocardiograms simulating posterior myocardial infarction after cessation of the tachycardia. It was shown that there were no constant structural or medicinal factors affecting the electrocardiograms. The return to normal was too rapid for a real occlusion. However, it is felt that the basis for the patient's pain and T changes was due to a temporary ischemia. This is another condition that can cause T-wave changes; it must be borne in mind because of the difference in

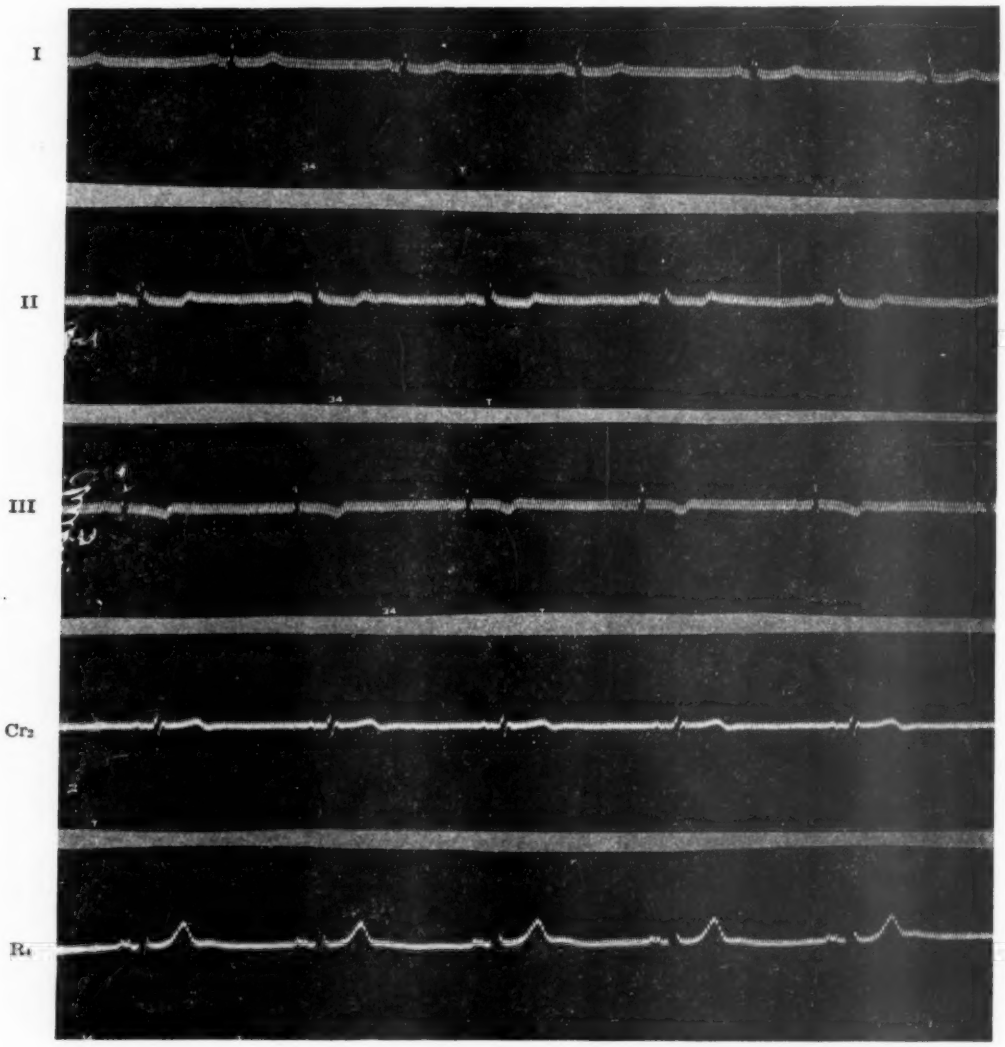

Fig. 3*B*.—This electrocardiogram, taken on Feb. 23, 1943, fifteen days after the second attack, shows T_2 and CR_2 to be diphasic and T_3 inverted. There is still notching in all QRS complexes.

prognosis. A careful and detailed history of the attack or attacks, progress studies, and the slight differences between this pattern and the usual coronary patterns will enable one to make a correct diagnosis and prognosis.

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HEART TUMOR: REPORT OF A CASE

MAJOR ROBERT A. STEVEN, M.C.

THIS case is reported because of several unusual features which made an accurate ante-mortem diagnosis difficult.

The patient was a 25-year-old soldier with no previous pertinent illness except for a questionable pneumonia in 1942. There was no history of rheumatic infection. His parents were living, and his father, aged 50 years, had heart disease. Two siblings were living and well.

The soldier first became ill on April 15, 1943, with anorexia, night sweats, cough, palpitation, shortness of breath, and loss of weight. Between then and May 1 he lost 12 pounds. He also had nonradiating retrosternal pain, described as an ache or a weight or pressure, associated with his shortness of breath. On May 1 he was admitted to an Evacuation Hospital and after five days developed a high fever, a rapid thready pulse, cyanosis, orthopnea, and peripheral edema. On May 5 he was transferred to Torney General Hospital where he was admitted to the Contagious Disease Section. The transfer diagnosis was lobar pneumonia involving the right lower lobe. He received 18 Gm. of sulfathiazole at the hospital. The white blood cell count on May 2 was 4,700 with 73 per cent polys, and on May 5 it was 4,550 with 80 per cent polys. Red counts on the same dates were 3.96 and 4.5 million.

On entry the nurse noted a pulse of 128, respirations of 28, and temperature of 102.2° F. Examination by the Chief of the Contagious Disease Section showed the following positive findings: scattered skin lesions on all extremities, some macular, others ulcerative, and some healed with thin scars (the dermatologist made a diagnosis of erythema multiforme); orthopnea and marked cyanosis of the face, neck, upper chest, and nail beds; injected throat and some post nasal drip; no adenopathy; normal thyroid; lagging of the right chest and dullness, diminished breath sounds, many fine râles at the right base, and a pleural rub in the axilla; pulse weak and thready with a rate of 144 per minute; gallop rhythm at the apex; no murmurs; heart sounds of fair quality; blood pressure 100/82; tender liver 5 fingerbreadths below the right costal margin; edge of the spleen palpable; 1 plus edema of legs but no sacral edema; neurological examination negative; no ascites.

Later in the day, I was asked to examine the soldier in view of his cardiac findings. There was orthopnea and some cyanosis of the fingers, toes, and face even when he was in the oxygen tent, although much less than when he was out of the tent. He was complaining of pain across the front of the chest and pain with deep breathing. The point of maximum intensity was just outside the mid-clavicular line in the left fifth intercostal space. There were no thrills or friction rub. There was a gallop rhythm at the apex. The sounds were faint at the apex, but much louder over the base. There was a rough, swishing, systolic murmur medial to the apex. The pulse rate was 144. The chest signs were as given previously. There was gross enlargement of both lobes of the liver and 1 plus edema of the feet and ankles. The preliminary impression was acute myocardial failure precipitated by pneumonia of undetermined etiology. The treatment instituted was rapid intravenous digitalization, salyrgan with theophyllin, whisky, and caffeine when necessary. He was also given sulfadiazine for several days because of the signs of pneumonia.

Blood: Red blood cell count, 3,610,000; hemoglobin, 85 per cent; white blood cell count, 5,250; neutrophiles, 70 per cent; lymphocytes, 29 per cent; eosinophiles, 1 per cent; morphology, normal. Sulfathiazole blood level was 6 mg. per cent. Urine: specific gravity, 1.032; albumin, negative; sugar, negative; Microscopic examination, normal except that crystals resembling sulfathiazole were present. Blood Kahn reaction was negative. Sputum was negative. A portable x-ray of the chest showed areas in the right upper and right base suggestive of consolidation, and considerable enlargement of the heart was suggested. His cardiographic tracing is seen in Fig. 1. Several red blood cell counts during the course of his illness showed a mild reduction, while others were within normal limits, but all the

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hemoglobin determinations were normal. Several sputa were negative for acid-fast organisms. Altogether six cardiograms were obtained, and all were essentially alike. Many urinalyses were done, and all were essentially negative except for albuminuria which varied from none to 1 plus.

Progress Notes.—May 6: Temperature, 98° F.; pulse, 116; peripheral edema nearly gone; liver, 3 fingerbreadths below the costal margin. No cyanosis was present while the patient was in the oxygen tent, and breathing was easier. Output during the night was 900 c.c., and sweating had been profuse. Eleven cat units of digitalis were administered intravenously in eighteen hours; also, 2 c.c. of salyrgan were administered intravenously. P_2 was accentuated. Gallop rhythm was gone. Some râles were present at both bases. The patient seemed greatly improved and very cheerful. His electrocardiogram indicated that posterior infarction was at that time a possibility.

May 7: All edema gone; pulse, still 112; liver, still smaller. Systolic apical murmur was at that time very faint and soft and blowing, due possibly to improvement in the cardiac dilatation. Sulfadiazine level was 19.6 mg. per cent.

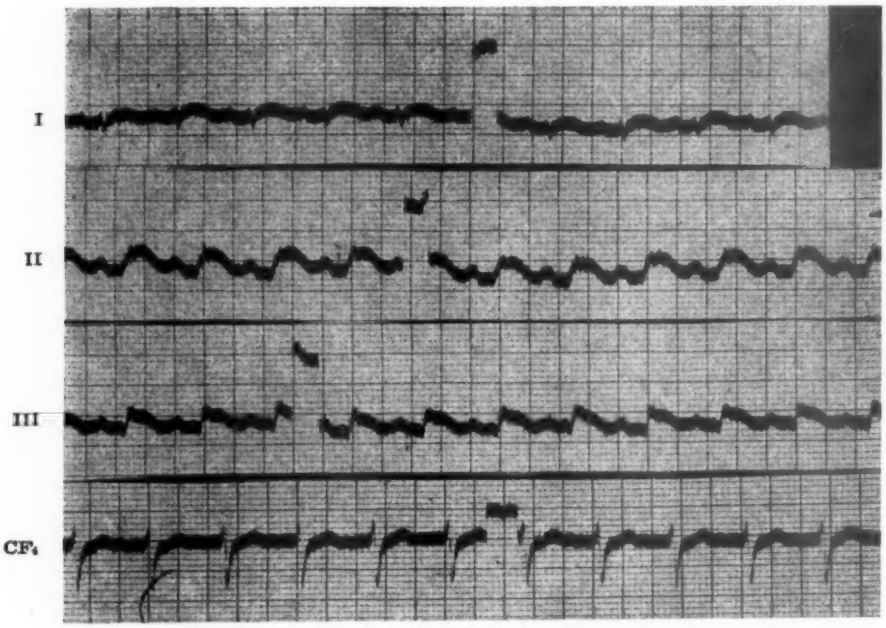

Fig. 1.—Electrocardiogram taken May 11, 1943.

May 8: Blood pressure, 92/58; pulse, 116; afebrile. Intake (twenty-four hours), 780 c.c.; output, 510 cubic centimeters. Cough gone. No edema.

May 9: Blood pressure, 80/60; pulse, 124 (paradoxical pulse); respirations, 16; temperature, 101° F. Later in the day the patient became very dyspneic; his blood pressure was 76/70. The heart sounds were faint. Tamponade of the heart was considered, and a pericardial tap was done. Ten cubic centimeters of clear yellow fluid were obtained which, in the light of further developments, was probably pleural transudate. Late in the day his temperature was 103.6° F., his pulse was 144; and his blood pressure was 102/70. The white blood cell count was 4,250 with 85 per cent polys.

May 10: Pulse, 144; respirations, 28; blood pressure, 112/88; sounds, distant; gallop rhythm present; no peripheral edema; liver down 2 fingerbreadths. The patient appeared critically ill. Morphine was started. The white blood cell count was 7,500 with 87 per cent polys. The sedimentation rate was 5.2 mm. per hour.

May 13: Dyspneic; cyanotic; pulse, 120; respirations, 28; blood pressure, 108/88; liver at level of navel. Blood culture (eighth day) was still sterile. Sulfadiazine was stopped. Maintenance doses of digitalis were continued. One plus edema was present; râles were heard at both bases. A paradoxical pulse was present. The area of cardiac dullness was widened. Some bloody sputum could be raised.

May 14: Six hundred cubic centimeters of serosanguineous fluid were removed from the left side of the chest. Nonprotein nitrogen was 72 mg. per cent. Salyrgan administration was stopped. Sulfadiazine level was 13 mg. per cent. Sedimentation rate was 20 mg. per cent. Smears and aerobic and anaerobic cultures of the pericardial (pleural) fluid were negative.

May 15: White blood cell count was 12,300 with 84 per cent polys. Three plus edema of the lower legs and sacrum was present.

May 17: Some coffee-ground emesis and abdominal distention were present. The blood pressure was 92/66, and the pulse was 120. The patient was getting steadily worse. White blood cell count was 8,700 with 86 per cent polys.

May 19: The patient continued to have coffee-ground emesis. During the preceding two days he had been given glucose intravenously. Nonprotein nitrogen was 103; creatinine was 2.2. He was given 250 c.c. of whole blood. The white blood cell count was 10,400 with 97 per cent polys.

May 20: Temperature, 99.4° F.; pulse, 116; blood pressure, 90/60; paradoxical pulse; gallop rhythm; a variable high-pitched diastolic murmur in the fourth intercostal space, and a to and fro soft systolic blow at the apex; Cheynes-Stokes respirations; râles at both bases; tender, questionably pulsating liver nearly to navel; slight peripheral edema and signs of ascites; pupils small and fail to react to light; tongue crusted and dry; and teeth and gums coated. He passed a tarry black stool. The white blood cell count was 10,850 with 94 per cent polys.

May 21: Shortly after intravenous administration of glucose the patient suddenly gave a gasp and died. A second blood culture, taken just before death, showed a growth of *Streptococcus viridans* four days later.

Autopsy Findings.—Positive findings only from the autopsy report follow. The pathologic diagnoses were concurred in by the Surgeon General's office.

Several maculopustular skin lesions, covered by thick crusts, varying from 1 to 3 cm. in diameter, were present on the chest and extremities. The liver was 3 fingerbreadths below the costal margin. About 100 c.c. of clear yellow fluid were present in the peritoneal cavity. On the serosa of the jejunum and ileum in the lymphoid tissue, opposite the attachment of the mesentery, were about eight whitish, sharply demarcated plaques, varying from 0.6 to 2 cm. in diameter, surrounded by indistinct hemorrhagic zones and induration. The vessels leading to these areas were prominent. The mucous membrane opposite each of these plaques was the site of an ulcer. All these ulcers were transverse, their edges were elevated and indurated, and in places, were covered with reddish black material. Sections through these ulcers showed massive infiltration by cells similar to those described in the heart below. Each pleural cavity contained 1 liter of clear yellow fluid. The heart was enlarged and prominently occupied the anterior mediastinum. The pericardial sac contained about 5 c.c. of clear yellow fluid. There were fibrinous adhesions between the pericardium and epicardium. The heart weighed 460 grams. The epicardium was rough and covered by a layer of shaggy fibrin. In several places, especially over the posterior surface of the left ventricle, the epicardium was whitish and greatly thickened. The right auricle was of normal size, and its endocardium was smooth. The foramen ovale appeared functionally closed but showed a slitlike opening which admitted a large probe. The right auricular appendage was empty. The coronary sinus appeared normal. The tricuspid valve and its chordae tendineae and papillary muscles were normal. The right ventricle was slightly dilated; its endocardium was smooth; and its muscle was quite pale with a yellowish-white tint in places. Cross sections show the myocardium to be replaced in several places by a soft homogeneous tissue which obscured the normal fibrillar structure of the myocardium. The pulmonary valves were normal. The pulmonary aorta contained a clot of blood. The left auricle was large; its endocardium was smooth; and its wall was thin. The left auricular appendage was empty. The mitral valve was normal in all respects. The left ventricle was greatly dilated. Its endocardium was smooth and showed many irregularly shaped, sometimes confluent, areas of yellowish-white discoloration. No thrombi were present. Cross section showed a yellowish-white tissue replacing much of the myocardial wall, and in such areas the fibrillar structure of the myocardium had entirely disappeared. These areas varied in size from small flecks to areas measuring 4 and 5 centimeters. This occurred in all parts of the heart including the inter-

ventricular septum. The aortic valve was normal in all respects. Except for occasional yellowish-white plaques on the intima of the larger branches, the coronary system was normal. The wall of the aorta was quite thin, and the lumen was comparatively small, especially the abdominal portion. There was an area of bluish-red discoloration on the posterior aspect of the left lower lobe and another on the medial margin of the left upper lobe, each measuring about 4 cm. in diameter. Cross section of the area in the lower lobe showed a wedge-shaped, blackish-red portion under the pleura. No thrombus or embolus was seen in the vessels below this area. The area in the upper lobe appeared as a typical hemorrhagic infarct. In the right lung several areas of bluish-red discoloration were seen under the pleura which on section seemed to be hemorrhagic infarcts. The spleen weighed 115 grams. The liver weighed 480 grams, and its consistency was firm. The gall bladder, pancreas, and adrenals were normal. The left kidney, ureter, renal artery, and seminal vesicle were absent. The right kidney weighed 180 grams and was grossly normal. The bladder contained no left ureteral orifice. The right seminal vesicle and the prostate were normal. The testes were normal.

MICROSCOPIC

Left Ventricle.—The serosal cells of the epicardium were mostly missing and replaced by thick strands of hyaline fibrin which was being organized. In a few places several layers of somewhat irregularly arranged serosal cells were present. The epicardium was greatly thickened due to the presence of edema, fibrin, granulation tissue, and infiltrations of lymphocytes, plasma cells, and monocytes. The subepicardial fat tissue was, in several places, densely infiltrated by tumor cells which were round or polyhedral in shape showing rather large, round or oval, chromatin-rich nuclei with indefinite nucleoli. The cells were fairly uniform but the nuclei varied somewhat in size, shape, and staining characteristics. Many mitotic figures were seen, some of which were quite irregular. The tumor cells had invaded the septa of the fat tissue and had replaced many of the fat globules. In one place tumor cells were seen to invade the epicardium and there was extensive invasion of the myocardium. Tumor cells were present, especially in the larger septa, but also about the individual myocardial fibers causing vacuolar degeneration, atrophy, and necrosis of many of the fibers. A papillary muscle seen in the section also showed massive invasion by tumor cells and a thick layer of tumor was present beneath the endocardium. The remaining portion of the myocardium showed moderately hypertrophied fibers with distinct striations. Most of the nuclei were vesicular, and there was a moderate amount of lipochrome pigment about the poles of the nuclei. A portion of the mitral valve showed edema but was otherwise normal. One lymphatic vessel seen in the subepicardial fat tissue contained tumor cells.

Right Ventricle.—Most of the myocardium was extensively infiltrated by tumor cells growing in a fashion similar to that described above. In a few areas the myocardium was entirely replaced by tumor. There was extensive necrosis of parts of the myocardium and of the tumor tissue. The lumina of several vessels of the myocardial septa were solidly filled with tumor cells; these vessels appeared to be lymphatic. The epicardium showed changes similar to those above. Again, as previously, muscle tissue of a papillary muscle showed massive invasion by tumor.

Interventricular Septum.—There was massive invasion of a portion of the septum by tumor, and in such places the heart muscle fibers show changes similar to those above. The septum was markedly thickened by edema. In places the endocardium was infiltrated by tumor. No Purkinje fibers were recognized.

With a Foot-Bielschowsky stain the argentophil fibers were well preserved except for small areas of necrosis where some of the fibers were broken up. There was no increase in reticulum fibers in the areas infiltrated by tumor. With the oxidase stain no oxidase granules were demonstrated in the tumor cells. The outer layer of the adventitia of the aorta was thickened and covered with masses of bulky hyaline fibrin which was being organized. Beneath this there was granulation tissue.

Except for hemorrhagic infarcts, edema, emphysema, and fibrinous pleurisy secondary to the infarcts, the lungs were clear.

Essential pathologic diagnoses were:

1. Multiple lymphosarcoma of the jejunum and ileum with metastases to the skin and heart.

2. Cardiac hypertrophy, subacute fibrinous pericarditis, and pleurisy, hydrothorax, passive hyperemia of spleen and liver, secondary to 1.

3. Congenital aplasia of left kidney, ureter, and seminal vesicle.

COMMENT

When the patient was first seen the outstanding clinical features were fever, leucopenia, physical and x-ray signs of pneumonitis, and obvious congestive heart failure, all of which were interpreted as virus pneumonia with secondary cardiac failure. Possibly the sulfonamide was the cause of the low white blood cell count. When the first electrocardiogram was seen, a posterior infarction was suggested by the elevated S-T segments in Leads II and III. Serial tracings failed to show the usual progression of changes seen in infarction. Clinical features then suggested cardiac tamponade, which was not verified by two taps. Tumor was not suspected. The primary lesions in the bowel gave rise to no symptoms except possibly the coffee-ground vomitus and tarry stool terminally, so that, from a diagnostic standpoint, the tumor was as difficult to discover as a primary cardiac neoplasm is.

No review of the literature will be given as there have been several in recent years, including one by Lisa and his co-workers.[1] Incidentally, their Case 1, a female, aged 17 years, also suffering from a metastatic lymphosarcoma, ran a course very similar to that of our case, although the electrocardiograms in the two cases were very different.

Intractable cardiac failure with no clear-cut etiology, mentioned by numerous writers as common in cardiac neoplasms, is again illustrated by this case. It was impossible, however, to definitely rule out rheumatic heart disease with mitral insufficiency.

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ACUTE RHEUMATIC HEART DISEASE IN THE AGED, WITH REPORT OF A CASE WITH STOKES-ADAMS SYNDROME TREATED WITH PAREDRINE

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ACUTE rheumatic heart disease is fairly common among young persons, but it is rare in the aged. The initial attack of rheumatic heart disease occurs between 5 and 11 years of age, according to the data of Leonard.[1] On the other hand, active rheumatic heart disease is rare after 50 years of age. Rothschild, Kugel, and Gross[2] found only two cases in the sixth decade of life and one in the seventh decade, and Rakov and Taylor[3] reported another case in the seventh decade. The purpose of this report is to record a case of an initial attack of rheumatic heart disease which developed at 64 years of age, was characterized by a Stokes-Adams syndrome of unusual severity, and was treated with paredrine, at times in large doses.

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CASE REPORT

A white man, aged 64 years, had always been well and had participated in vigorous physical activity. His principal hobby was mountain climbing, and he took long hikes daily. On Nov. 12, 1942, he noted headache, generalized aching, and painful muscles and joints, particularly of the lumbar region and wrists. Three days later he consulted one of us (A. W. B.), at which time his temperature was 102° F. The wrists were not red, hot, or swollen. During the next two weeks the fever and aching persisted, but the joint manifestations moved to the shoulders, hips, knees, and ankles. The manifestations subsided during the third week of the illness, and he was permitted to be out of bed for increasing periods daily. During the evening of December 2, he walked into another room, became unconscious, and fell. The attack occurred without warning, and subsided very soon after he had fallen. A few minutes later nothing abnormal could be ascertained by physical examination, except a contusion of the scalp from the fall. At approximately 3 o'clock the following morning, he was awakened by a "pecular feeling," and, during the next few minutes, was observed to have three convulsions of only a few seconds' duration. Physical examination a few minutes later revealed nothing unusual. The pulse was regular and of normal rate and contour, and the blood pressure was 140/80. During the next three hours five more convulsions were observed; they were characterized by jerking of the arms and hands, slight opisthotonos, and labored respiration. They lasted approximately five seconds, and occurred without warning, without loss of sphincter control, and without demonstrable residual manifestations. The attacks became more frequent, occurring every few minutes, and asystole was found to be present during the attack. A diagnosis of Stokes-Adams syndrome was made, and he was admitted to Mercy Hospital, in Iowa City, Iowa. An electrocardiogram, Fig. 1, showed periods of complete auriculoventricular block, with ventricular asystole.

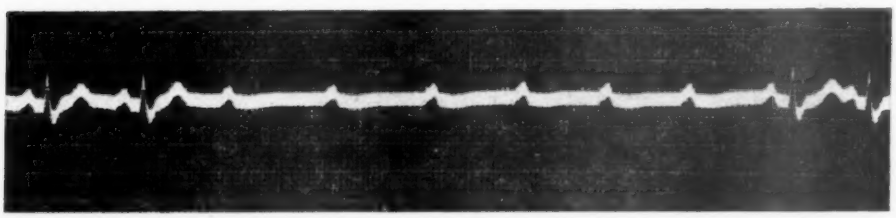

Fig. 1.—Complete auriculoventricular block, with periods of ventricular asystoles, are seen in Lead II the morning of the first day in the hospital.

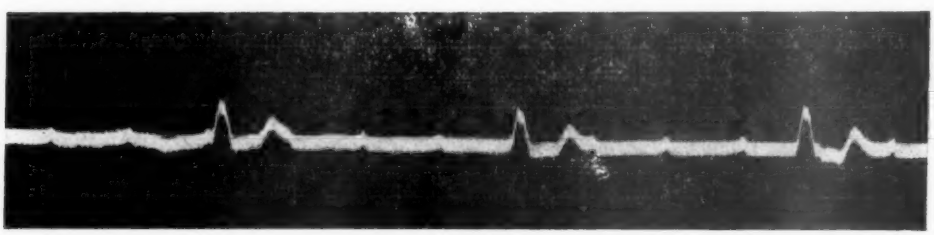

Fig. 2.—Complete auriculoventricular block and left bundle branch block are observed in Lead I on the afternoon of the first day in the hospital.

The intravenous administration of 7½ grains of theophyllin ethylenediamine, and the oral and subcutaneous administration of ¾ grain of ephedrine did not decrease the frequency of the attacks. Convulsions continued at three- to five-minute intervals, and lasted fifteen to thirty seconds, for four hours. At this time paredrine, in doses of 60 mg., was administered orally every two hours. After the third dose, four hours later, the convulsions became less frequent and of shorter duration, and one and one-half hours later they ceased. An electrocardiogram, Fig. 2, revealed complete auriculoventricular block, with delayed conduction in the left branch. An abnormally high T wave in Lead IV, Fig. 3, indicated myocardial disease. The complete heart block continued for two days, when it changed to a two-to-one auriculoventricular block (Fig. 4). During this time he received 1,320 mg. of paredrine, or approximately 500 mg. daily. At approximately noon of the third day the pulse rate suddenly increased to 130 beats per minute and became irregular. An electrocardiogram confirmed the diagnosis of auricular fibrillation. Paredrine was discontinued, but the fibrillation continued

until noon of the following day, at which time the pulse rate decreased to 90 beats per minute and became regular. An electrocardiogram showed normal mechanism. Paredrine therapy was resumed, and 240 mg. were administered during that afternoon and evening. Auricular fibrillation recurred and disappeared six hours after paredrine was discontinued. The following day paredrine was resumed in doses of 60 mg. three times daily.

During the second day in the hospital the temperature began to rise, and it reached 102° F. the next day. The respirations increased to 40 per minute, the right shoulder became painful and tender, and the patient became irrational. Within ten hours after the institution of salycylate therapy, the temperature and respirations had returned to normal, but during the next five days the temperature rose to 99.6° F. in the afternoon, and the ankles became very tender. During the next eight days he became rational and the joints gradually improved.

The cardiac manifestations had apparently become stabilized, with normal mechanism, but the systolic arterial pressure had risen to 170 mm. Hg. The dose of paredrine was reduced to 40 mg. three times daily, and two days later to 20 mg. four times daily. At approximately noon on this day, the thirteenth day in the hospital, convulsions recurred and continued at two- to three-hour intervals for the next three days. An electrocardiogram showed frequent periods of ventricular asystole, interrupted by numerous ventricular extrasystoles. Convulsions, very probably, would have been more frequent if it had not been for these ventricular extrasystoles. The temperature rose to 102° F., and paredrine was resumed in doses of 100 mg. five times daily. Convulsions ceased two days later, and the following day the temperature returned to normal. Nothing of significance occurred for twenty-two days, during which time paredrine was continued in the doses mentioned. An electrocardiogram obtained during this time showed delayed conduction in the right branch of the bundle.

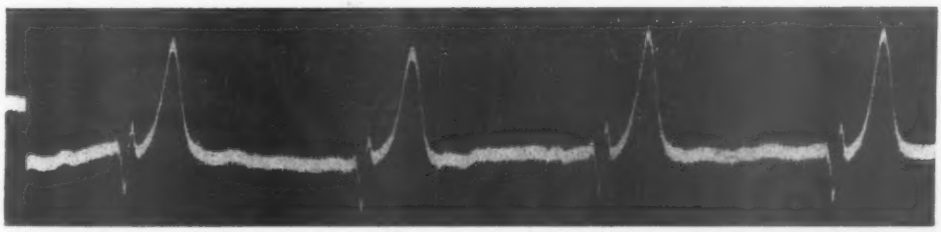

Fig. 3.—The abnormally high T wave in Lead IVF on the morning of the second day in the hospital.

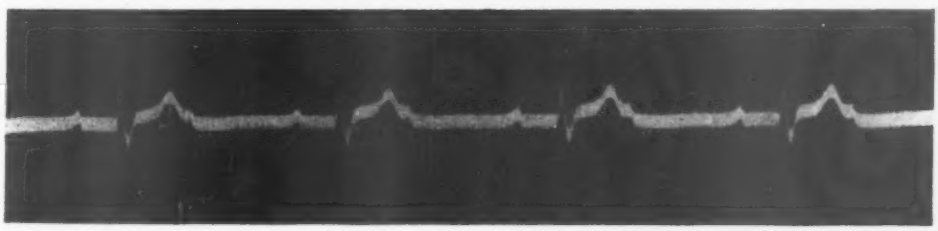

Fig. 4.—The two-to-one auriculoventricular block in Lead I on the morning of the third day in the hospital.

Convulsions and fever returned at approximately 7 A.M. on the thirty-eighth day in the hospital, or twenty-three days after the last recurrence. The convulsions occurred at approximaterly hourly intervals and lasted ten to twenty seconds. During the first day of this recurrence the paredrine was increased from the usual 500 mg. to 1,400 mg., and, in addition, 2 c.c. of epinephrine in oil were administered intramuscularly. An electrocardiogram revealed periods of ventricular asystole, interrupted by frequent ventricular extrasystoles. The next morning the cardiac condition was unchanged, and the convulsions continued. In spite of this, all medication was discontinued in the hope that complete auriculoventricular block would develop and the periods of asystole and convulsions would cease. The convulsions decreased and ceased at approximately 4 P.M. that day, but the pulse continued irregular, with short periods of ventricular asystoles for the next five days. The temperature remained elevated to 100° F. for the next four days, and then gradually returned to normal.

During the second day of this recurrence the ankles, knees, and wrists became red, hot, swollen, and extremely tender. The manifestations gradually subsided except that the electro-

cardiogram continued to show delayed conduction in the right branch of the bundle. He was discharged from the hospital on the sixty-seventh day, and remained in bed at home for three and one-half months, at which time an electrocardiogram, Fig. 5, showed the Wilson S-type of right bundle branch block and a grossly abnormal Lead IVF. He gradually increased his activity for one year without evidence of recurrence.

The leucocyte count was 17,000 upon admission to the hospital, declined to 10,700 at the time of discharge, and has remained from 7,000 to 8,000 since. The erythrocyte count, hemoglobin, and urine were normal throughout his illness, and the blood Wassermann reaction was negative.

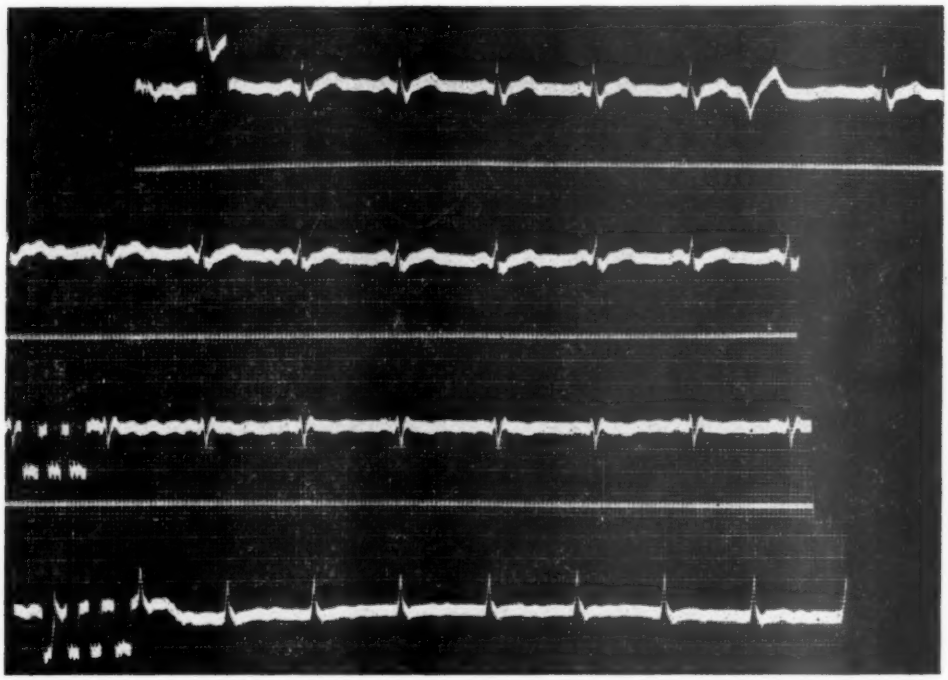

Fig. 5.—The Wilson S-type of right bundle branch block and grossly abnormal curve in Lead IVF are seen in the electrocardiogram taken three and one-half months after the last recurrence.

COMMENT

Lesions in the auriculoventricular node have not been prominent in the reported cases of rheumatic heart disease in the aged. Delayed conduction, on the other hand, is fairly common in younger persons. The Stokes-Adams syndrome is extremely rare in rheumatic heart disease at any age. It is difficult to ascertain in our case whether or not the auricular fibrillation and ventricular extrasystoles were due to the rheumatic heart disease or to the paredrine.

Nathanson, Engelberg, and Hersh[4] reported encouraging results with the use of paredrine in the treatment of heart block. Of their six cases, partial block was eliminated in one of two cases, the ventricular rate was increased in the other, and the block was changed from complete to partial in two of four cases. They administered 60 mg. of paredrine three times daily, and emphasized that the pressor effect was less than with other preparations of this series of drugs. The oral administration of 80 mg. of paredrine increased the systolic pressure an average of 69 mm. Hg, and the duration of the effect was two hours. They pointed out that the stimulating effect upon the conduction of the heart was relatively greater with this preparation, but they employed small doses as compared to those employed in our case. They stated that the drug is destroyed

in the gastroenteric tract in some cases, and that the drug is unsuitable in such instances.

It is difficult to evaluate the effect of paredrine in our case. The apparent improvement following the initial administration of the drug was due to the development of complete heart block, and not to the elimination of the block. Was the auricular fibrillation which developed after three days of over 500 mg. of paredrine daily due to the paredrine or to the rheumatic heart disease? The fact that the arrhythmia disappeared the day after discontinuing paredrine and recurred after the medication was resumed, and then disappeared again after the therapy was stopped for the second time, suggests that the drug was the exciting cause. On the other hand, doses of over 500 mg. of paredrine were resumed eight days later and continued for twenty-six days without producing auricular fibrillation. It appears, therefore, that the rheumatic fever was the principal factor in the production of the auricular fibrillation. We must consider, however, that it is possible that the drug was effective at first and later it became destroyed in the gastroenteric tract and was ineffective.

It appears doubtful that the drug was a factor in the production of the ventricular extrasystoles. During the second recurrence, the thirteenth day in the hospital, the dose had been reduced to only 80 mg. daily, and ventricular extrasystoles were prominent. In addition, ventricular extrasystoles continued during the last recurrence for five days after the drug had been discontinued. The fact that these disturbances in conduction occurred each time during reactivation of the rheumatic fever is additional evidence that the disease and not the drug was the principal factor in their production.

The largest dose of paredrine we have been able to find in the literature is 400 mg. daily, which was administered by Korns and Randall.[5] In their case this dose controlled the hypotension without the nervous stimulation which was experienced with benzedrine. They did not observe any unusual effect upon the conduction in the heart. Because of the pressor effect of paredrine, we were hesitant to use such large doses, but the increase in arterial pressure observed at the initial administration of the drug, i.e., from 140 to 170 mm. Hg, was the greatest increase which we observed.

SUMMARY

A case is reported in which the initial attack of rheumatic heart disease occurred at 64 years of age, and was characterized by complete heart block and a Stokes-Adams syndrome of unusual severity and duration; the latter was treated with unusually large doses of paredrine.

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Abstracts and Reviews

Selected Abstracts

Shore, R., Holt, J. P., and Knoefel, P. K.: Determination of Cardiac Output in the Dog by the Fick Procedure. Am. J. Physiol. **143**: 709, 1945.

The oxygen content of blood frequently differs when drawn simultaneously from the two venae cavae, from two points in the right auricle, or from the right auricle and right ventricle in dogs in barbital anesthesia. Estimation of cardiac output in the barbitalized dog by the Fick procedure with blood taken from the right auricle may be in considerable error as a result of obtaining a nonrepresentative sample of mixed venous blood.

There is a progressive decrease in cardiac output during the first four hours of barbital anesthesia in dogs.

AUTHORS.

Fenning, C., and Mott, C. R.: The Effect of Modulated High Frequency Condenser Field on the Straub-Fuehner Frog Heart Preparation. Am. J. Physiol. **144**: 1, 1945.

Characteristic cardiac and ventricular standstill of the Straub-Fuehner frog heart can be produced using modulated, high-frequency current applied in the manner shown by the authors.

The results so obtained show a selective action of the current, the specific nature of which is not understood. It is believed that the selective action takes place on the nerve terminals, the pacemaker, and the associated conductive system. Selective heating may account for the results, since it is known that a high frequency electrostatic field will preferentially heat oils faster than salines. In addition, there is some evidence of chemical factors produced or activated during exposure.

AUTHORS.

Duomarco, J., Rimini, R., and Recrate, P.: Intraabdominal Pressure and the Pressure in the Inferior Vena Cava. Rev. argent. de cardiol. **11**: 273, 1945.

In dogs, optical records were obtained simultaneously of the pressure in the abdominal cavity and the pressure of the inferior vena cava, at various levels, and of the right auricle.

The forms and absolute values of both curves are identical when the venous pressure is taken just below the diaphragm; at more distant levels there is a small difference due to the vis a tergo.

Over the diaphragm the venous pressure declines suddenly, and cardiac waves appear in the record which is then practically identical with the record of intrathoracic pressure obtained after a partial pneumothorax.

The pressure variations of the abdominal and thoracic cavities are reciprocally blocked at the level at which the inferior vena cava crosses the diaphragm; this block disappears when the vein is abnormally distended.

AUTHORS.

Brannon, E. S., Merrill, A. J., Warren, J. V., and Stead, E. A., Jr.: The Cardiac Output in Patients With Chronic Anemia as Measured by the Technique of Right Atrial Catheterization. J. Clin. Investigation **24**: 332, 1945.

Twenty-four sets of data were obtained on eighteen anemic subjects. Atrial pressure readings and samples of mixed venous blood for determination of the cardiac output were obtained through a catheter introduced into the right atrium. The femoral arterial pressure was recorded optically by the method of Hamilton.

No consistent change in the circulation was observed when the hemoglobin level was above 7 Gm. per 100 milliliters. Below that level, the cardiac output at rest was increased, the arteriovenous oxygen difference and the peripheral resistance were decreased. The atrial pressure was not changed.

In four patients, observations were made before and after the hemoglobin had been doubled by transfusion or by the administration of liver extract. In each patient, the pulse rate fell, the diastolic and mean arterial pressures and peripheral resistance rose, and the cardiac output decreased.

When the hemoglobin level falls below 7 Gm. per 100 ml., the requirements of the body for blood are increased. This explains why anemic subjects may have circulatory insufficiency manifested by either shock or heart failure, while the heart is pumping as much as, or more than, would be required by a normal subject under similar conditions.

AUTHORS.

Warren, J. V., Brannon, E. S., Stead, E. A., Jr., and Merrill, A. J.: The Effect of Venesection and the Pooling of Blood in the Extremities on the Atrial Pressure and Cardiac Output in Normal Subjects With Observations on Acute Circulatory Collapse in Three Instances. J. Clin. Investigation **24**: 337, 1945.

The effect on the circulation of the removal of 300 to 900 ml. of blood by venesection and the effect of pooling of blood in the extremities by the venous tourniquets were studied in twelve normal men. The atrial pressure readings and the samples of mixed venous blood for measuring the cardiac output were obtained through a catheter introduced into the right atrium by way of the antecubital vein. The femoral arterial pressure was recorded optically.

Venesection and the application of venous tourniquets caused a fall in atrial pressure from 20 to 65 mm. of water. There was no consistent change in cardiac output, mean arterial pressure, or peripheral resistance. Returning the blood by transfusion or by releasing the venous tourniquets was followed by a return of the atrial pressure to the control level without any change in the cardiac output.

The data suggest that the normal atrial pressure with the subject in the recumbent position is somewhat in excess of that required to fill the ventricles and that a decrease in blood volume of the degree reported here produces a lowering of atrial pressure without interfering with ventricular filling. These observations obviously do not apply to massive hemorrhage.

Acute circulatory collapse appeared in three instances. The subjects became pale, sweated profusely, and complained of nausea and weakness. The pulse rate slowed strikingly. The atrial pressure increased, the cardiac output remained unchanged. There was a marked fall in the arterial pressure and peripheral resistance. The circulatory collapse appeared to be the result of a sudden decrease in peripheral resistance because of reflex vasodilatation, presumably in the arterioles. There was no evidence of a decreased venous return.

AUTHORS.

Vizcaíno, M., Pallarés, D. S., and Cabrera, E.: Certain Considerations Concerning Electrocardiogram Type S_1 S_2 S_3. Arch. Inst. Cardiol. Mex. **14**: 261, 1945.

The authors studied the electrocardiograms of twenty clinically normal persons, fourteen persons with normal hearts and some other extracardiac process, and sixteen cardiac patients.

They confirm the findings of Ashman and Hull in regard to the normality of Types S_1 S_2 and S_3 and conclude that the majority of the tracings with low voltage are normal, even X, though they fail to fulfill the requirements postulated by the aforementioned authors, providing there is no other anomaly (other than low voltage). The examination should include careful study of the unipolar leads VR, VL, and VF and the precordial leads.

AUTHORS.

Hoff, H. E., and Nahum, L. H.: The Electrocardiographic Localization of Myocardial Infarcts by Injury Currents and Ventricular Extrasystoles. Am. J. Physiol. **143**: 723, 1945.

Myocardial damage was produced in four regions of the dog heart by means of appropriate ligation of coronary arteries. These were (a) right and left ventricles exclusively, and (b) anterior and posterior regions involving adjacent portions of the right and left ventricles.

The changes in the S-T segment of the electrocardiogram in Leads I and III were the same as produced by potassium chloride injury in the same regions, namely, (a) depressed S-T segment with right ventricular damage, (b) elevated S-T segment with left ventricular damage, (c) elevation of S-T and depression of $S\text{-}T_3$ with anterior damage, and (d) depression of $S\text{-}T_1$ and elevation of $S\text{-}T_3$ with posterior damage.

The ventricular extrasystoles which appeared spontaneously after coronary occlusion showed configurations which indicated that they originated within the damaged area. They showed S-T segment changes which were the same as in the supraventricular complexes. Their configuration in the electrocardiogram may therefore serve as a localizing sign in myocardial damage.

AUTHORS.

Sabathié, L. G., Gaspary, F. V., and Rojas, R. A.: Unstable Intraventricular Block. Rev. argent. de cardiol. **11**: 297, 1945.

Fourteen cases of nonpermanent intraventricular block were studied clinically and electrocardiographically. The denomination of "unstable" intraventricular block was adopted for these cases, classifying them as transitory or intermittent according to the circumstances.

In the mechanism of production of these blocks the modification of the refractory periods in both branches of the His bundle are of fundamental importance; the role of the precipitating factors, such as increased heart rate and vagal action, is also pointed out.

AUTHORS.

Leys, D. G.: Heart Block Following Diphtheria. Brit. Heart J. **7**: 57, 1945.

The evidence that this case of complete heart block was due to diphtheria is: (1) the patient had severe diphtheria with neuritis at the age of 10 years; (2) subsequently a slow pulse was reported at the age of 22 years; and (3) she has complete absence of all tendon jerks without other evidence of nervous system disease.

AUTHOR.

Gómez, B. H., and Yépez, C. G.: Permanent Auricular Fibrillation in Two Brothers Without Evidence of Organic Heart Disease. Arch. Inst. Cardiol. Mex. **14**: 251, 1945.

The authors present two cases of auricular fibrillation in brothers without apparent cardiac injury and without other evident cause. In other similar observations published, there also are no explanations to justify the alteration of the cardiac rhythm.

AUTHORS.

Pruitt, R. D., Barnes, A. R., Essex, H. E.: Electrocardiographic Changes Associated With Lesions in the Deeper Layers of the Myocardium. Am. J. M. Sc. **210**: 100, 1945.

Myocardial injuries were produced in dogs by mechanical means. Damage to the endocardium and deeper layers of the myocardium of the apical portion of the left ventricle was attended by certain changes in the configuration of the QRS complex in a precordial lead designated apical IVR. Most constant among these changes was a reduction in the height of the R wave. The development of a Q wave or a notch low on the upstroke of the R wave were alternative types of change.

These changes in the QRS complex might be derived from: (1) injury to, or destruction of, the myocardial fibers adjacent to the endocardium; or (2) damage to Purkinje's network or the larger subdivisions of the left branch of the bundle of His.

Although in each of the twenty-two experiments under analysis there was accomplished an extensive destruction of those tissues in which portions of Purkinje's system are supposed to lie, in twenty experiments the width of the QRS complex remained unchanged. The speed at which the excitatory impulse was propagated apparently remained essentially unchanged, even though its course, as indicated by the form of the QRS complex, was altered. Also, a lesion high on the septum apparently not only is attended by a widening of the QRS complex, but also it is the only lesion likely to produce this effect.

Our results indicate that surface lesions exert a dominant influence on the level of the RS-T segment. We have suggested that this circumstance may prevail not because the traumatized subendocardial fibers fail to produce currents of injury, but because the resulting injury potentials are masked by the normal action currents arising in the uninjured superficial fibers in response to the excitatory process.

Changes in the T wave following injuries to the deeper layers of the myocardium were inconstant. The most frequently recurring alternation was an inversion of the T wave in a lead designated apical IVR.

AUTHORS.

Cameron, D. R.: Transient Heart Block and Coronary Occlusion in Pleural Shock. Brit. Heart J. 7: 104, 1945.

In the case here described, heart block existing during the acute phase may have been due partly to a vagal reflex; yet a more important factor, from the subsequent cardiogram, would appear to have been a coronary occlusion. The possibility of acute coronary insufficiency without occlusion, as described by Master (1944), is not a likely one; his cardiograms do not resemble those here described. It is hardly likely that a coincident coronary thrombosis took place. The close association with the attempted pneumothorax induction, together with the age of the patient, make this extremely unlikely. A wound of the heart can be excluded; the needle was never deep enough to have produced this. A clot disturbed from a thrombotic process in the pulmonary circulation might produce an embolism (Saphir, 1933), and this remains a possibility. It seems more reasonable to assume that an air embolism occurred.

As the typical changes indicative of coronary occlusion may take some little time to develop—up to a few hours (White, 1931)—this right axis deviation may have existed before the accident, as in Durant's case.

An interesting point is the absence of pain. Pain is evidently not one of the main features of this form of pleural shock. It may be that this absence of pain is a clinical characteristic of coronary air embolism, in contradistinction to other types of occlusion.

Heart block may occur more commonly in pleural shock than is thought, and Cocke remarks on bradycardia in two of his cases.

It is suggested that, in the case here reported, coronary air embolism occurred producing transient heart block and myocardial infarction.

AUTHOR.

Groedel, F. M., and Miller, M.: The Nature and Origin of the So-Called Systolic Gallop Rhythm. Exper. Med. & Surg. 3: 107, 1945.

Five cases with an apical mesosystolic click in the phonocardiogram and a slight displacement of the heart shadow in the x-ray film were demonstrated. In the cardiogram, the click was more like a murmur than a sound and appeared, distinctly, somewhat earlier over the vessels of the neck than at the apex of the heart. It was, therefore, obvious that the click originated in the close proximity of the heart, probably mostly in the larger pulmonary arteries. The cause of the click, in such cases, is most probably some constriction in this area, on the basis of minor pulmonary processes, which may occur during youth (calcified glands or minor pleuritic or pulmonary processes).

AUTHORS.

Bloomfield, A. L., Armstrong, C. D., and Kirby, W. M. M.: The Treatment of Subacute Bacterial Endocarditis With Penicillin. J. Clin. Investigation 24: 251, 1945.

Intensive penicillin therapy over long periods (approximately six to eight weeks) led to the following results in eleven patients with bacterial endocarditis caused by strains of streptococcus sensitive in the test tube.

All patients were promptly made "bacteria-free" (blood cultures) except one who died early in the course of treatment. Eight, or 73 per cent, were clinically cured of the infection after follow-up periods up to six months. One patient, apparently cured of the infection, died of cardiac failure. Cocci were seen in the depths of a scarred mitral valve. The significance of this observation is not clear. There were no clinical relapses or reinfections. Petechiae and emboli continued for some time after the blood cultures were negative. Renal lesions as evidenced by studies of urinary sediment were not as a rule completely eliminated by the treatment.

AUTHORS.

Dolphin, A., and Cruickshank, R.: Penicillin Therapy in Acute Bacterial Endocarditis. Brit. M. J. 1: 897, 1945.

Six cases of acute bacterial endocarditis—three due to hemolytic streptococcus, two to *Staphylococcus aureus,* and one to hemolytic streptococcus were treated with moderate doses of penicillin. Four of the patients were alive six to twelve months after penicillin therapy was stopped; three were well, and one had improved.

Attention is directed to the frequency of infection of healthy heart valves by streptococcus, which not uncommonly causes mild genital-tract sepsis, particularly after abortion.

The criteria for the diagnosis of acute bacterial endocarditis which may occur during the course of a generalized infection are discussed.

AUTHORS.

Arrillaga, F. C.: Segmentary Pericarditis. Arch. Inst. Cardiol. Mex. 14: 225, 1945.

A description is given of the radiographic features of the pericarditis that develop when the pericardium has adhesions or partitions produced by previous pericardial episodes (segmentary pericarditis). Four varieties may be distinguished, which yield characteristic radiologic pictures: the *left, right, superior,* and *inferior* segmentary pericarditis. The x-ray pictures supply the evidence of this classification.

AUTHOR.

Keith, J. D., and Ross, A.: Observations on Salicylate Therapy in Rheumatic Fever. Canad. M. A. J. 52: 554, 1945.

The oral administration of 13.3 Gm. (200 grains) of sodium salicylate with an equal quantity of sodium bicarbonate produces an average blood level of 31 mg. per cent. Ten grams (150 grains) of sodium salicylate with sodium bicarbonate produces a blood level averaging 27 mg. per cent.

Such levels are sufficient to control joint symptoms, keep the temperature down, and reduce the pulse rate. The sedimentationn rate returned to normal in an average of four weeks in the group on 10 to 13.3 Gm. of salicylate and four and one-half weeks in the group on 0 to 1.7 Gm.

The incident of heart disease was approximately the same in the high salicylate group as in the low salicylate group. The numbers were not adequate to draw unequivocal occlusions. Ten per cent of the rheumatic patients who entered the hospital with normal hearts developed rheumatic heart disease that could be recognized at the time of discharge.

Nausea, vomiting, and tinnitus are much more common early in the administration of salicylates than after the patient has been receiving the drug for several days. These symptoms are not usually sufficient cause for stopping treatment. There was no evidence of kidney damage in this series. Three patients had toxic reactions characterized by hyperpnea. One of these might be labeled severe.

AUTHORS.

Fullerton, C. W.: The Prevention of Acute Rheumatic Fever. Canad. M. A. J. 52: 559, 1945.

Administration of 0.5 Gm. of sulfadiazine twice daily prevented the recurrence of acute articular rheumatism. This experience has been observed in 250,000 sailors during the winter months. The salicylates prevented the residual effects if they were continued long after an attack of rheumatism. The subjects treated prophylactically with sulfadiazine have been equally protected against scarlet fever and meningococcus meningitis.

AUTHOR.

Taran, L. M., and Jacobs, M. H.: Salicylate Therapy in Rheumatic Fever in Children. J. Pediat. 27: 59, 1945.

Rheumatic polyarthritis responds promptly and effectively to large doses of salicylates. This result can be attained by both oral and intravenous use of salicylates. The intravenous route in our series of cases did not seem to offer significant advantages over the oral route provided the same plasma salicylate level is reached. No difficulty was encountered in reaching the desired plasma level with oral salicylate administration. The technical difficulties and the annoying symptoms ever present in the intravenous method of therapy in our experience outweigh the possible benefits derived from this method of shortening slightly the period during which rheumatic activity exists. Massive doses of salicylates in this group of cases did not present any thrombopenic disturbances and failed to show any detectable evidence of acidosis.

Massive doses of salicylates used in rheumatic carditis in children seem to produce equally prompt and effective results. The sedimentation rate returns to normal as promptly as in the polyarthritic group provided the therapy is instituted at the onset of rheumatic

activity. When therapy is postponed, the subsidence of the rheumatic process is delayed for many weeks. All other signs of carditis, however, subsided at the same time as the sedimentation rate returned to normal. Intravenous therapy in this group may be hazardous.

Small doses of salicylates do not seem to affect the course of rheumatic carditis. The carditis seems to follow the same course whether insufficient doses of salicylates are given or salicylate therapy is completely withheld. The duration of the active process as measured by the presence of an elevated sedimentation rate is much longer than in the group receiving massive doses of salicylates. Furthermore, when salicylates are withheld or given in small doses, the rheumatic process shows evidence of activity for a long period following the return of the sedimentation rate to the normal level.

AUTHORS.

Book Reviews

ENFERMEDADES DEL CORAZON—CIRUGIA Y EMBARAZO: By Ignacio Chavez, Director del Instituto Nacional de Cardiologia, México, D. F. Edición de el Colegio Nacional, Mexico City, 1945, 182 pages.

The author of this monograph is the director of the National Institute of Cardiology of Mexico City. He presents the results of personal experience in addition to extensive bibliographic quotations.

The book is well written and gives interesting and important data on two "borderline syndromes" of Cardiology, as it deals with pregnancy and surgery as a source of risk for the cardiac patient. It includes a detailed analysis of the hemodynamics of normal pregnancy and indications for the management of complications during labor and during surgical interventions.

The electrocardiographic changes and the auscultatory signs of normal pregnancy, the action of different hypnotics, and the pathogenesis and treatment of pulmonary embolism are some of the many interesting points of this book.

A. LUISADA.

VOLUNTARY HEALTH AGENCIES: By Selskar M. Gunn and Philip S. Platt. Ronald Press Co., New York, 1945, 364 pages, $3.00.

Announcement

Due to conditions beyond the control of the editors and publishers, several issues of the JOURNAL are printed on an inferior grade of paper. Just as soon as the standard good grade of paper is available, its use will be resumed.

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THE American Heart Association is the only national organization devoted to educational work relating to diseases of the heart. Its activities are under the control and guidance of a Board of Directors composed of thirty eminent physicians who represent every portion of the country.

A central office is maintained for the coordination and distribution of important information. From it there issues a steady stream of books, pamphlets, charts, films, lantern slides, and similar educational material concerned with the recognition, prevention, or treatment of diseases of the heart, which are now the leading cause of death in the United States. The American Heart Journal is under the editorial supervision of the Association.

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The income from membership and donations provides the sole financial support of the Association. Lack of adequate funds seriously hampers more intensive educational activity and the support of important investigative work.

Annual membership is $5.00. Journal membership at $11.00 includes a year's subscription to the American Heart Journal (January-December) and annual membership in the Association. The Journal alone is $10.00 per year.

The Association earnestly solicits your support and suggestions for its work. Membership application blanks will be sent on request. Donations will be gratefully received and promptly acknowledged.